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Psychological factors in asthma outcomes: A Research Portfolio

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Thesis Portfolio Overview

This thesis follows the research portfolio format and is carried out in partial fulfilment of the academic component of the Doctorate in Clinical Psychology at the University of Edinburgh. In two chapters, the portfolio aimed to explore the role of psychological factors in asthma morbidity outcomes in adults with asthma. **Chapter One** includes a systematic review of published research literature exploring the relationship between emotion regulation strategies and asthma morbidity outcomes in the adult population. **Chapter Two** presents an empirical study examining the role of generalised anxiety in asthma outcomes and how experiential avoidance and self-efficacy influence this relationship. Both chapters have been prepared for submission to the Journal of Asthma according to its guidelines: https://www.tandfonline.com/action/authorSubmission?show=instructions&journalCode=ijas20

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Thesis Portfolio Abstract

Despite enhancements in medical asthma treatments, the disparity in asthma outcomes remains a pressing issue in asthma care and represents a significant personal burden for individuals living with asthma. To further improve available care, it is crucial to better understand which psychological factors might account for such disparity and the mechanisms through which they operate. In two chapters, the current research portfolio aimed to explore the role of psychological factors in asthma morbidity outcomes in adults with asthma.

The first chapter is a systematic review exploring the relationship between six emotion regulation strategies: acceptance, avoidance, problem-solving, reappraisal, worry/rumination and suppression and asthma outcomes: asthma control, health-related quality of life (QoL), health care utilisation and medication compliance in adults with asthma. A systematic search of four electronic databases resulted in 18 studies which met the inclusion criteria. The systematic review highlighted significant relationships between emotion regulation strategies and asthma outcomes. The direction of these relationships depended on the type of emotion regulation strategy and the asthma outcome studied. Findings from the current review highlighted that psychological interventions aimed at promoting more adaptive emotion regulation skills in adults with asthma might positively influence their asthma morbidity outcomes. Further research is needed, using improved methodological design and a clearer conceptualisation of emotion regulation construct.

The second chapter presents an empirical study. It explored the role of generalised anxiety (GA) in asthma outcomes: asthma QoL, asthma control and short-acting asthma reliever medication use (SAARM) and the potential mediation role of experiential avoidance (EA) and asthma control self-efficacy (SE). A cross-sectional set of questionnaires was completed by 65 participants attending NHS outpatient respiratory clinics. Correlation and mediation path analyses were conducted. Higher GA was associated with poorer asthma outcomes, lower asthma control SE and higher EA. After controlling for covariates, both SE and EA were found to mediate the relationship between GA and both asthma control and QoL. Neither SE nor EA played a mediatory role in the relationship between GA and SAARM use. These results need to be replicated in research using a longitudinal design. However, they provide preliminary support that psychological interventions targeting asthma control SE and EA could promote better asthma control and QoL in adults with asthma and co-morbid anxiety.

Layperson summary

Despite better available asthma medical care, people vary greatly in how they fare with asthma. To further improve available care, it is important to understand which psychological factors might influence these differences and how. In two chapters, the current research portfolio aimed to explore the role of psychological factors in asthma outcomes in adults with asthma.

Chapter one: Systematic review

Asthma is a chronic condition which is often linked with life adjustments, difficult self-management routines and unpleasant physical symptoms which are hard to predict. This can cause people living with asthma to experience many difficult emotions. Although the way people manage difficult emotions (a concept known as emotion regulation) has been linked with poorer illness outcomes in other chronic health conditions, asthma research is lacking.

We have reviewed available studies on emotion regulation and asthma outcomes such as asthma control, health-related quality of life (QoL), use of health services and use of asthma medication as advised. We have specifically looked at 6 common ways to regulate emotions such as: accepting, avoiding, reframing them in a positive light (a concept known as positive reappraisal), actively trying to approach the problem which causes the negative emotion (problem-solving), suppressing and worrying/ruminating (going over negative thoughts in one's head). The review aimed to see whether people who use different ways of regulating emotions fare better or worse with their asthma. We looked at studies with adults with asthma who were aged 16 and over.

The review showed that how people fared with asthma depended on the emotion regulation strategy they used. Avoiding, suppressing, and worrying were linked with worse asthma outcomes, whilst positively reappraising, accepting and expressing emotions were noted in people with better asthma outcomes. The results suggested that treatment supporting people with asthma to better manage their emotions might be useful to improve their asthma outcomes. We do however need more research to be confident of these findings.

Chapter two: Research study

Many people with asthma have generalised anxiety (frequent and uncontrollable worries about many different things) and this has been linked to poorer asthma control, poorer asthma-related QoL and the need to use asthma reliever medication more often. But the reason for this link is unclear.

In the research study, we tried to find out whether lower confidence in managing asthma (construct known as self-efficacy) and greater tendency to cope by avoiding unpleasant physical and emotional symptoms (construct known as experiential avoidance) can explain how anxiety can lead to poorer asthma outcomes. We were interested in people with asthma between 16 and 65 years old who were attending routine NHS asthma clinics. 65 people participated in this study. They filled questionnaires that measured levels of generalised anxiety, experiential avoidance, self-efficacy and asthma outcomes.

The results showed that people with higher levels of generalised anxiety reported poorer asthma outcomes. Those with higher levels of generalised anxiety also noted having lower self-efficacy to manage their asthma and a greater tendency to use experiential avoidance. Lower levels of self-efficacy and higher levels of experiential avoidance were found to influence the relationship between higher anxiety and poorer quality of life and asthma control but not asthma reliever medication use. These findings could not be better explained by other influences such as taking more steroid medication, living with asthma for longer or higher reliever medication use. More research is needed to confirm these findings. However, it suggests that treatments focusing on self-efficacy to manage asthma and experiential avoidance might help improve asthma outcomes in adults with generalised anxiety.

Chapter One: Systematic review

The relationship between emotion regulation strategies and indicators of asthma morbidity: a systematic review

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Abstract

Aim: The current systematic review aimed to explore the relationship between six emotion regulation strategies: acceptance, avoidance, problem-solving, reappraisal, worry/rumination and suppression and asthma morbidity outcomes (asthma control, health-related QoL, health care utilization and medication use) in the adult population with asthma. Method: A systematic search of electronic databases (EMBASE, PsychINFO, PsychARTICLES and MEDLINE (through the OVID electronic search interface) resulted in 3615 studies, of which 18 met the full inclusion criteria. Key information, including the relationship between emotion regulation strategies and asthma morbidity outcomes were extracted and each study was appraised and rated in terms of its methodological quality and risk of bias. Results: The systematic review highlighted significant relationships between emotion regulation strategies and asthma outcomes. The direction of these relationships depended on the type of emotion regulation strategy and the asthma outcome studied. Discussion: Findings from the current review highlight that psychological interventions aimed at promoting more adaptive emotion regulation skills in adults with asthma might be beneficial in improving their asthma morbidity outcomes. Further research is needed, using improved methodological design and a clearer conceptualisation of emotion regulation construct.

Keywords: Asthma; health; illness management; quality of life; acceptance; avoidance; problem-solving; reappraisal; rumination; suppression

1. Background

Asthma is a chronic respiratory illness often characterised by recurrent inflammation of airways and physical symptoms such as a tight chest, wheezing, shortness of breath and coughing [1]. It is estimated that in the UK 4.3 million adults are currently receiving treatment for asthma [2]. Although asthma is a condition that can be managed very successfully through self-management and medication, it is estimated that in the UK around 1200 people a year die because of asthma [3] and more than 50% live with asthma which is poorly controlled [4]. Poor asthma control was associated with worse outcomes with regards to mortality, asthma-related quality of life (QoL) and higher utilization of health services in the UK sample of adult

asthmatics [4]. To further improve available care and to reduce the individual and economic impact of asthma, it is crucial to better understand factors which might account for such disparity.

It is well established that chronic illness including asthma is often accompanied by on-going health threats, unpleasant physical symptoms, and life adjustments [2,5]. Additionally, individuals with asthma are required to adopt complex self-management health behaviours which place further demands on their cognitive and emotional processing. These include managing the physical symptoms of asthma (e.g. medication adherence, health care visits) as well as maintaining positive well-being and QoL [2]. The burden of asthma symptoms as well as the self-management demands, often lead to increased levels of anxiety, stress as well as other arrays of difficult emotions, which are often more prevalent than in healthy adults [2, 7-10]. Psychological factors including anxiety and stress have previously been linked to poorer health outcomes in chronic illness including asthma [7,11]. However, less is known about underlying mechanisms accounting for such relationships.

The processes which individuals with chronic health conditions use to regulate their emotions has been suggested as one possible mechanism to explain the link between negative emotions and disparity in health outcomes [12-13]. Emotion regulation is defined as a self-regulatory effort to modulate which emotions we feel, when we feel them, how we feel them and express them [14]. It has been suggested that illness-related emotional demands can deplete individuals' resources to self-manage their illness, intensify, and prolong the experience of physical symptoms leading to poorer health outcomes [15-16]. Indeed, research in chronic illnesses such as fibromyalgia and cancer found that maladaptive emotion regulation was associated with more physical symptoms, higher health care utilization and poorer well-being [17-19]. This highlights the importance of exploring processes involved in an optimal modulation of responses to difficult emotions to better understand their impact on health-related behaviours and health outcomes. It is vital to recognise that optimal emotion regulation does not involve erasing difficult emotion or replacing them with positive ones. Instead, it requires individuals to adjust their responses to difficult emotions in a way that produces more adaptive responses and choices, leading to better illness outcomes [20-21].

Previous literature on emotion regulation in the chronically ill population has mainly focused on exploring its association with health outcomes in conditions such as cancer, diabetes, HIV and chronic pain [22-23]. Similar research exploring emotion regulation in the asthma population is more limited [22]. Individuals living with

asthma and associated difficulties are likely to experience a different type of illness stressors in a specific context. This will inherently impact on how individuals regulate their affective experiences. Indeed, individuals with asthma were found to use strategies to manage their emotions which differed from those with other chronic illnesses [24]. This is in line with both the emotion regulation model by Aldao [20] and the model of coping [25] which both highlight the context-specific nature of the emotion regulation process. Exploring emotion regulation processes specific to asthma population is therefore needed to gain more representative account.

Concerning the current systematic review, it is important to note that emotion regulation as a construct has been described as complex, lacking consistent conceptualisation and comprehensive measurement across different studies [26]. Emotion regulation also significantly overlaps with other constructs such as coping. Although these have traditionally been studied separately, they both highlight the crucial role of using controlled set regulatory processes to modulate the frequency, magnitude or content of a wider range of affective, behavioural and physical responses [e.g. 14,27-28]. Whilst coping mainly focuses on modulating negative affect in response to a stressor, emotion regulation is theorized to occur to regulate any type of affect in response to any situation [14, 28]. Despite this, coping uses similar modulatory processes (cognitive, behavioural, situational and emotional) and can be viewed as a subcategory of emotion regulation occurring under stress [29]. The conceptual overlap between individual strategies measured by both coping and emotion regulation instruments have also been highlighted in previous research [20,31]. These strategies include problem-solving, reappraisal, acceptance, avoidance, emotional suppression and worry/rumination [20,32].

To our knowledge, only one systematic review looked at coping and health outcomes in an asthma population. In their review, Barton et al. [24] found that among individuals with asthma the use emotion regulation strategy of avoidance, including affective avoidance strategy of denial, were associated with higher emergency care use and hospitalisations. However, the evidence for these relationships relied only on a small subset of studies (n=4) with two of these employing qualitative design. This review reported mixed results for the association between avoidance and medication adherence. These results were based on a limited number of studies (n=2). One study reported that individuals labelled as “deniers” reported more over-use of reliever medication and under-use of preventer medication compared to “accepters” and “pragmatists”. Individuals reported their medication use to be linked with their styles of regulating their emotions. More general avoidance was not found to be associated

with medication adherence in the only included quantitative study exploring this relationship. Barton et al. [24] concluded that more research is needed to identify which emotion regulation strategies are associated with more optimal asthma health outcomes. This will inform us which specific components to include and target when designing future asthma interventions.

Because of this considerable overlap between coping and emotion regulation, studying these independently has often been difficult. Given the clear advantages of being able to collectively examine different affect regulatory processes across asthma research, specific emotion regulation strategies measured by subscales within either emotion regulation or coping measures will both be included in the present review. For the current review, emotion strategies will be defined as processes through which individuals consciously modify the magnitude and/or the type of their emotional experience or events which elicited those experiences [30]. The current review will focus on six categories of emotion regulation strategies, namely emotion suppression, avoidance, acceptance, rumination/worry, a problem-solving and positive reappraisal. These categories were reported in a recent systematic review by Aldao et al. [30] and were previously theorized to measure overlapping constructs across both coping and emotion regulation research [31]. For a definition of these emotion regulation categories please see Appendix AA. Although these will provide a helpful framework to review relevant emotion regulation strategies, it is important to note that these reflect only a small subset of strategies which adults with asthma might employ to manage their emotional experiences. The current systematic review will focus on adult asthma population to allow comparison with previous systematic reviews.

Given the previously highlighted gaps in the emotion regulation literature, the current systematic review aims to expand on previous work by synthesising and critically appraising research on emotion regulation and health outcomes in adult asthma population. Specifically, it will focus on exploring which emotion regulation strategies are linked with better/poorer asthma morbidity indicators such as QoL, health care utilisation, medication adherence and markers of asthma control.

2. Methods

Search strategy

A systematic review was conducted in October 2019, searching the following electronic databases: EMBASE, PsychINFO, PsychARTICLES and MEDLINE (through the OVID electronic search interface). The search strategy used a combination of each emotion regulation strategy and type of health outcome in adult asthma population. These included the following broad terms and associated MeSH subject headings: "accept*", "avoid*", "reapprais*", "suppress*" "problem-solv*", "ruminat*", "emotion* regulat*", "emot* dysregulat*, "self-manag*","asthma quality of life" and "asthma*". The search was limited to articles published between 1985 and 2019, available in English or Czech and involving humans. A full search strategy used is outlined in Table 1 in Appendix A. The reference list of identified articles was hand searched for additional relevant studies. A protocol for the current systematic review was registered with the International Prospective Register of Systematic Reviews PROSPERO on 31/10/19 before article search and data extraction. It can be found at: https://www.crd.york.ac.uk/PROSPERO/display_record.php?RecordID=149928.

Study selection

Studies were eligible for inclusion if they reported data regarding a relationship between one or more of the following emotion regulation strategies: (acceptance, avoidance, problem-solving, reappraisal, rumination, suppression) and at least one of the following primary asthma outcomes of interest: self-reported and physiological indicators of asthma control, asthma medication adherence and asthma/or health-related QoL. Studies were defined as assessing an indicator of asthma control if they included a validated measure of asthma control (e.g. ACT and ACQ) or measured one of the following key expressions of asthma control as defined by Global Initiative for Asthma guidelines such as day/night symptoms, physical activity limitations, exacerbations, or lung function (measured by e.g. forced expiratory volume in one second (FEV_1) or peak expiratory flow rate (PEFR) [30]. Study selection was limited to studies which employed a validated measure of an emotion regulation strategy, in line with specific subscales detailed in a recent meta-analysis by Aldao et al. [30] and which were conducted in adults 16+ years old with a diagnosis of asthma. Studies were excluded if they only included a general emotion regulation score and data regarding specific subscales could not be obtained. Studies addressing both adults and children were eligible for inclusion if adult data were reported separately or if the mean age of

the recruited sample was at least 16 years. Studies involving adults with comorbid health conditions which may have had influenced their memory, such as dementia and Parkinson's disease were excluded. Studies using a population with co-morbid substance misuse difficulties were also excluded as substances can act as a form of emotion regulation (e.g. experiential avoidance). Single case studies and qualitative design studies were excluded. Dissertations, theses, poster presentation and conference abstracts were included if they included enough detail about the study methodology or further information was obtained from contacting authors or manual searches.

Data extraction and synthesis

The author (LM) independently examined the search output and screened it by title and abstract. Using the outlined inclusion criteria, the full texts of potentially eligible studies were retrieved and assessed further for eligibility. Data were extracted from eligible studies regarding sample characteristics, emotion regulation strategy characteristics, study methods and data on the relationship between specific emotion regulation strategy and specific asthma control outcomes of interest. Detailed data extraction form can be found in Appendix B. Authors were contacted, where necessary, for further information.

Assessment of study quality

The current review employed the Downs and Black checklist [34] (Appendix C) to appraise the methodological quality of the included studies. This checklist has been adapted to appraise four areas of methodological quality, specifically: external validity, internal validity: bias, internal validity: confounding (selection bias) and power. Within these areas, six criteria were considered for each selected study: (i) the representativeness of the study sample; (ii) the use and reporting of "data dredging" (iii) the appropriate use of statistical tests to assess outcomes; (iv) the appropriate use of outcome measures; (v) the adequate adjustments for confounding in the analyses from which the main findings were drawn; (vi) the sufficient power of the sample to detect clinically significant effects where the reported difference had less than 5% probability to occur by chance. Please refer to Appendix D for more details regarding the adapted checklist.

Using the above criteria, selected studies were rated by the author (LM). A third of the included studies were randomly selected to be rated by a second reviewer (GOH). A disagreement between reviewers was discussed and resolved by consensus. Selected articles were rated according to whether they appropriately addressed (1

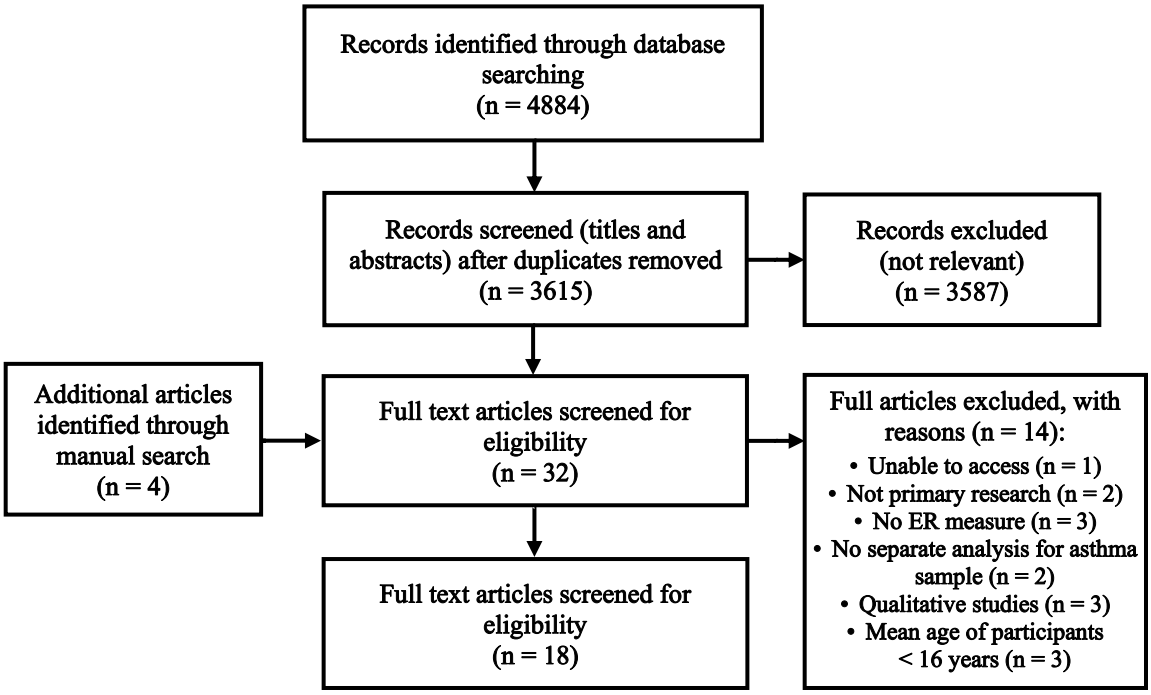
point) or did not address/unable to determine (0 points) each criterion. A total score for each study was then calculated. Scores were used to categorise studies as being of good (A), satisfactory (B) or poor methodological quality (C) (Appendix E).

3. Results

Search results

The search and the screening procedure identified 18 full-text articles which met the inclusion criteria and were eligible for data extraction. See Figure 1 for the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flowchart [35].

Figure 1: PRISMA flowchart of the literature search and screening process



Study characteristics

The characteristics of eligible articles and key findings are presented in Table 1.1. and 1.2. respectively. Articles were each assigned a study number. This study number will be used to refer to articles in the following sections.

One study appeared twice, as each article used different analysis and investigated different primary outcomes [S2,4]. Six of the 17 included studies were conducted in the USA [S12,13,14,15,17,18], five in Australia [S2/4,3,5,8], three in Spain [S7,9,10], two in Netherlands [S6,11] and one study each in Poland [S16] and Finland [S1].

All studies in the present review were quantitative with a majority using a cross-sectional design (12 studies) [S1,5,6,7,10,11,12,13,14,16,17,18]. Additional four studies were longitudinal [S2/4,9,15] and assessed correlation or similar relationship between predictor at baseline and outcome of interest at follow up. In most cases, the variables were assessed at 12 months follow up. One study included a control group [S8] and one consisted of prospective RCT [S3]. Data regarding a relationship between emotion regulation strategy at baseline and primary/secondary outcomes at 12 months follow up were extracted from the RCT study.

Overall, the 17 studies had a total of 5515 participants (at baseline), where 10 of these reported <100 participants each. The sample sizes ranged from 14 to 3496 participants. Most studies recruited participants who were at least 16-18 years of age with a maximum age cut off for participation ranging from 60-75years. Six studies included no maximum age criteria for participation [S2/4, 5 14,16,17,18]. The sample mean of studies focusing on adults with asthma range ranged between 34.7 – 49 years. The broadest age range reported in this review was between 18-89 years [S16]. Two studies focused on a younger demographic group of school and college students and reported sample mean age between 16.24 – 19.5 years [S6,12].

Eight studies in this review recruited subjects from secondary and tertiary asthma care settings. Three of these studies included participants attending hospital outpatient Immuno-allergy/pneumology [S7,9,10] and pulmonary clinics [S14], inpatient wards [S16] or a combination of both [S2/4, 3]. One study employed a sample presenting at the Accident and Emergency (A&E) department [S5]. Only one study recruited their subjects from Primary care settings, namely GP practices [S11]. Three studies employed a community sample of individuals with asthma, two recruited from school and university college settings [S6,12] and one study used general asthma population [S1]. Study 15 used a convenience sample recruited from public/private pulmonary clinic, community chest clinic, general population, and college.

Most of the reviewed studies used a validated method to establish an asthma diagnosis. These included a diagnosis made by a physician (12 studies) [S2/4,3,5,6,7,10,11,14, 15,16,17,18], often in combination with an objective measure such as spirometry or PEFR, objective measures such as spirometry or PEFR only [S8] and a social insurance register record for an asthma medication reimbursement [S1]. One study established asthma diagnosis through a self-report only [S13] and one used a combination of a self-report and an asthma screening questionnaire [S12]. Ten out of 14 studies included participants with moderate to severe asthma. In 4 included studies, the severity of asthma was not reported or indicated [S8,13,17,18].

6 studies reported exclusion criteria relating to other respiratory, physical illness or/and psychiatric comorbidities [S7,9,10,11,14,18], often without giving a reason. In adults with asthma approximately 3.4% of 18-54years old and 12% of over 55 years old present with physical, psychiatric or other respiratory comorbidities [36]. These comorbidities in adults with asthma have previously been linked with poorer health outcomes such as asthma control, higher health care utilisation and lower QoL [37]. Not considering comorbidities when investigating asthma health outcomes in the above studies can be restricting the representativeness and generalisability of the recruited samples.

In the 18 included articles, the most frequently measured emotion regulation strategy was avoidance (reported in 11 studies), followed by problem-solving (8 studies), acceptance and emotion suppression/expression (measured in 5 studies each), positive reappraisal (3 studies) and rumination/worry (2 studies). Selected emotion regulation measures varied greatly across studies. The most employed instrument was Coping Orientations of Problems experienced (COPE) questionnaire [38] and Illness behaviour questionnaire (IBQ) [39], each used in three studies.

Most measured asthma morbidity outcome in this review was asthma control (including indicators of asthma control) (10 studies), followed by HRQoL (9 studies), health care utilisation (6 studies), and medication compliance (2 studies).

Table 1.1. Key characteristics of included studies

	Study no; Author &Year	Study sample: Population, Size, Gender %, Age (years) (SD, range), Asthma control/severity (%/mean, SD)	Type of ER	Measure	Primary and Secondary Outcome	Measure
1.	**Aalto et al. [40] Finland**	General population N = 3496 Female = 63% Age: 44.6 ±13.5 Asthma severity:(self-rated scale (0-10): 4.6 ± 2.1 (Mild symptoms)	1. **EA/ACCEPTANCE** Ignoring asthma (**cognitive EA**) Hiding asthma (**behavioural EA**) 2. **POSITIVE REAPPRAISAL:** Positive reappraisal subscale 3. **PROBLEM-SOLVING** Information seeking 4. **RUMINATION/WORRY** Asthma worry subscale	All - WCAEL [40] developed from Asthma Coping Scale [38]	1. **HRQoL (general):** Psychological and Physical health dimension 2. **HCU** 3. **ASTHMA CONTROL** (symptom severity)	1. RAND-36 [42] 2. Frequency (past year): (a) GP asthma visits (b) Nurse asthma visits 3. The severity of symptoms and their impact on daily activities/sleep (0-10)
2.	**Adams et al. [43] Australia**	Consecutive hospital in/outpatients (including those visiting A&E) N = 293 (212 at 12m F/U) Age: 42 ± 18 Female: 67% Asthma severity (NAEPP criteria): 58% severe asthma	1. **EA/ACCEPTANCE:** **a. Avoidance coping** (incl. cognitive EA: wishful thinking, and behavioural items). **b.** Denial (**affective EA**) 2. **PROBLEM-SOLVING:** (incl.: planning and information seeking)	1a. Avoidance coping subscale [44] 1b. Denial subscale – IBQ [39] 2. Active coping scale [44]	1. **HCU**	1. Self-reported frequency in the past 12m (collected at 3m intervals): (a) Hospital admissions (b) A&E visits
3.	**Adams et al. [45] Australia**	Hospital in/outpatients N= 131 (88 at 12m F/U) Age: 37.3; Female: 60% Asthma severity (FEV1%pred): 75.8± 18 (moderate asthma)	1. **EA/ACCEPTANCE** Denial (**affective EA**)	1. Denial subscale - IBQ [39]	1. **HCU**	1. Self-reported frequency: (a) A&E visits (b) Hospital admissions
4.	**Adams et al. [46] Australia**	Same sample as [S2] but different analysis N = 293 (232 at 12m F/U) Age: 42 ± 18 Female: 67% Asthma severity (NAEPP criteria): 58% severe asthma	1. **EA/ACCEPTANCE:** a. Avoidance coping (incl. cognitive-behavioural EA items) b. Denial (**affective EA**) 2. **PROBLEM-SOLVING:** (incl.: planning and info. seeking)	1a. Avoidance coping subscale [44] 1b. Denial subscale - IBQ [39] 2. Active coping scale [44]	1. **HRQoL:** a. Asthma specific b. General	1a. MAQLQ-M [47] 1b. SF-36 [48]: • Physical Component Summary (PCS • Mental Component Summary (MCS)

5.	**Campbell et al. [49] Australia**	Hospital Patients who presented in the hospital A&E with a near-fatal asthma attack N = 77 Age: 38.2± 2.2 Male: Female ratio: 1.41:1 Asthma severity: 58.1% of sample severe asthma	1. **EA/ACCEPTANCE** Denial **(Affective EA)**	1. denial scale - IBQ [39]	1. **HCU** 2. **ASTHMA CONTROL** a. Symptom severity b. Function limitation	1. Self-reported frequency): (a) doctor visits ♦ (b) A&E visits ♦ (c) hospital admissions ♦♦ (d) ICU admissions ♦♦ 2a. self-reported asthma severity score [48] ♦♦: score incl.: symptoms, no of asthma attacks, exercise capacity, medication and HCU. b. self-reported daily activities limitation
6.	**Cillessen et al. [51] Netherlands**	School population N=94; Female 41 out of 94 Age: 16.24±1.02 (14-18) Asthma severity: N/R. Excluded: not using daily preventative medication	1. **EA/ACCEPTANCE:** Trait acceptance	1. The CAMM (8/10 items measure acceptance of experiences) [52]	1. **HRQoL** (asthma specific) 2. **ASTHMA CONTROL**	1. AAQoL [53] 2. ACQ [54]
7.	**Fernandes [55] Spain**	Hospital outpatients (Immunoallergology) N = 195; Female: 76.4% Age:38±14.5 (17-75) 66.2% severe persistent asthma; FEV1%pred: 83.5± 22.4 (19%-120%) Excluded: Psychiatric clinical cases. 80.9% had atopy and 60.3% of the sample had rhinitis.	1. **EA/ACCEPTANCE:** Hiding asthma (**behavioural EA**) 2. **WORRY/RUMINATION:** Worry subscale 3. **POSITIVE REAPPRAISAL:** Positive reappraisal subscale	1-3. WCAEL [40]	1. **HRQoL** (asthma specific): 2. **ASTHMA CONTROL**	1. MiniAQLQ [56] 2. ACQ [54]
8.	**Ford et al. [57] Australia**	Clinical sample N = 14; Female: 57.1% Age: 47.5 (27-60) Asthma severity: N/R Excluded: hypertension and/or other complicating comorbidities	1. **EA/ACCEPTANCE:** Avoidance subscale (cognitive, affective and behavioural EA items) 2. **PROBLEM-SOLVING:** Positive coping (current condition)	1. Avoidance subscale IES [58] 2. Positive coping style subscale; AAS [58]	1. **MED. COMPLIANCE**	1. Compliance with controller asthma medication (any taken). Separate scores based on structured interview questions and a tablet count

9.	**Gonzales et al. [60] Spain**	Hospital Outpatients (tertiary allergy and pneumology clinics) N= 75 Female: 65.3% Age: 37.52±15.02 (18-72) Asthma severity (GINA and self-reported): 55 and 40 (moderate to severe) Excluded: comorbid physical/psychiatric illness	1. **EA/ACCEPTANCE:** (a) Acceptance (b) Denial **(affective EA)** (c) Distraction **(Cog.-beh. EA)** 2. **PROBLEM-SOLVING**: Planning and Active Coping 3. **POSITIVE REAPPRAISAL:** Positive Reinterpretation 4. **EE/SUPPRESSION:** (expression of negative emotions)	1-4. COPE subscales [38]: 1a. Acceptance 1b. Denial 1c. Distractive Activities 2. Planning and Active Coping 3. Positive Reinterpretation 4. Venting emotions	1. **HCU**	1. Frequency of asthma-related visits during 12m F/U: (a) Emergency room (b) Hospital acute exacerbations
10.	**Gonzales-Freire et al. [60b] Spain**	Hospital Outpatients (tertiary allergy and pneumology clinics) N = 373; Female: 70.5% Age: 36.88 ± 14.90 Asthma control (ACT, GINA): 57.7%, 65.6% well controlled; 42.2%, 4.9%uncontrolled. Comorbid physical/psychiatric illness excluded (except rhinitis)	1. **EA/ACCEPTANCE** Cognitive avoidance subscale 2. **PROBLEM-SOLVING:** Cognitive coping of the problem subscale	1. COPE [38]: (denial, turning to religion, mental disengagement) 2. COPE [38]: (planning and active coping + active steps to remove stressors + (-) retirement of coping	1. **HRQoL:** a. Asthma specific b. General	1a. SGRQ [61] 1b. SF-36[62]
11.	**Hesselink et al. [63] Netherlands**	Primary care (GP) surgeries N=220; Female: 70% Age: 45.0±14.1(16-75) Asthma severity (FEV1%pred): 93.1 ±14.9 (mild asthma); comorbid pulmonary/terminal illness excluded	1. **EA)/ACCEPTANCE** (illness specific): Avoidant coping style 2. **PROBLEM-SOLVING:** Rational/Problem coping style	1. Disease-specific coping questionnaire [64-65]: incl.: a tendency to avoid, ignore, deny, or minimise the seriousness of a problem. 2. Rational/Problem coping style	1. **HRQoL** (asthma specific):	1. QLRIQ [66]
12.	**Kraemer and McLeish [67] USA**	Undergrad. Psychology students N = 56; Female: 69.6% Age: 19.5±2.7 (18–37) Asthma control (ACT): 22.62±2.91(well-controlled)	1. **EA/ACCEPTANCE:** Acceptance 2. **EE/SUPPRESSION:** EE with labels	1. Non-judgment subscale FFMQ [68] 2. Describing subscale FFMQ [68]	1. **ASTHMA CONTROL**	1. ACT [69]
13.	**Kraemer and McLeish [70] USA**	Community sample N=61; Female: 61.9% Age: 34.7±13.6 (18-65) Asthma control (ACT): 15.98±4.54 (poor control), smokers excluded	1. **EA/ACCEPTANCE:** Acceptance 2. **EE/SUPPRESSION:** EE with labels	1. Non-judgment subscale FFMQ [68] 2. Describing subscale FFMQ [68]	1. **HRQoL** (asthma specific): 2. **ASTHMA CONTROL**	1. AQLQ [71] 2. ACT [69]
14.	**McCormick et al [72] USA**	Hospital outpatients (pulmonary clinic) N = 44; Female: 82.5% Age: 49.0±14.7 (20-78) Asthma control (ACQ): 1.92±1.2 (poorly controlled) Excluded: >1 respiratory diagnosis	1. **PROBLEM-SOLVING:** a. Rational PS style b. A constructive PS style c. Impulsive-careless PS style 2. **POSITIVE REAPPRAISAL:** Positive problem orientation Negative problem orientation	1-2. SPSI-R [73]	1. **HRQOL** (asthma specific) 2. **ASTHMA CONTROL**	1. MiniAQLQ SF [56] 2. ACQ [54]

15.	**McGann et al.[74] USA**	A convenience sample - public/private pulmonary clinic, community chest clinic, general population and college students. N=51 Female: 82.4% Age: 42 ±14.99 Asthma severity (FEV1 %pred): 77± .26 (moderate asthma); 54.9% of the sample in the two highest NHLBI severity categories	1. **EA/ACCEPTANCE:** (a) Cognitive denial subscale (b) Affective denial subscale	1. LDIS (asthma specific) [75-76]: (a) incl.: symptoms and somatic concerns displacement, minimization of diagnosis/prognosis, avoidance of information and health problems (b) incl.: denial of sleep problems, anxiety, depression, anger, fear of death, detachment/indifference)	1. **ASTHMA CONTROL** (lung function) 2. **MEDICATION COMPLIANCE** (objective)	1. FEV1%pred 2. Micro-electronic monitor (inhaled controller medication)
16.	**Mroczek et al. [77] Poland**	Hospital inpatients – two pulmonology wards N=172; Female:39.5% Age: 58 (18-89) 14% comorbid COPD Asthma severity (FEV1%pred): 78.5% of patients ≥ 60 (mild asthma)	1. **EA/ACCEPTANCE** Acceptance of illness	1. AIS [78]	**HRQoL** (general): **HCU**	1. WHOQoL-BREF [79] Polish version (Physical, Psychological, Environmental and social relationship domains) 2. a) HCU Index (past 12m) b) No. of hospitalisations (last 3y)
17.	**Nazarian et al. [80] USA**	A community sample of adults with asthma N=61; Female:67.2% Age: 42 ±14.13 (18-77) Asthma severity (PEFR): 389.98 ± 98.38 Excluded: asthma-related emergency treatment in the past 3m.	1. **EA/ACCEPTANCE:** (a) Mental disengagement (cognitive EA) (b) Behavioural disengagement (c) Denial (affective EA)	1. COPE [38]	1. **ASTHMA CONTROL** a. symptom severity b. lung function	1a. Asthma symptoms (coughing, interference from asthma and restrictions resulting from asthma). Prompted to record 5x/day for 1w using EMA procedure. 1b. PEFR
18.	**Russel et al. [81] USA**	Community adults with asthma N = 97; Female: 72% Asthma severity (PEFR): 346.07 ± 102.37 Age: 42.3±14.09	1. **EE/SUPPRESSION:** Anger expression and suppression	1. Anger in and Anger out subscales - STAXI [82]	1. **ASTHMA CONTROL (symptom severity)** Physical limitations due to asthma: interference with daily routine and restriction of activities	1. Disease-specific symptom severity (using EMA)

m=months; y=years; w=week CS=Cross-sectional; LT=Longitudinal; CC=Case-control; RCT=Randomized controlled trial
Child and Adolescent Mindfulness Measure (CAMM); Coping Orientations to Problems Experienced Inventory (COPE); St George's Respiratory Questionnaire (SGRQ); 36-Item Short-Form Health Survey. (SF-36); Asthma quality of life questionnaire (AQLQ); Five facet mindfulness questionnaire (FFMQ); Mini Asthma Quality of Life Questionnaire -Short Form (MiniAQLQ-S); Social Problem-Solving Inventory-Revised: Short Form (SPSI-R: S); Asthma Control Questionnaire (ACQ); Impact and Event Scale (IES); Active Approach set (AAS); Asthma Coping Scale (ACS); The Levine Denial of Illness Scale (LDIS); The Quality of Life in Respiratory Illness Questionnaire (QLRIQ); A&E – Accidents and Emergencies; ICU – Intensive Care Unit. Asthma control Test (ACT) (patient-rated asthma control), GINA – clinician-rated asthma control; HCU – Health Care Utilisation; PEFR – Peak Expiratory Flow Rate; EMA – Ecological Momentary Assessment; Modified version of the Mark's Asthma Quality of Life Questionnaire (MAQLQ-M); Asthma Coping Scale (ACS); EE – Emotion expression; Impact of Events Scale (IES); State-Trait Anger Expression Inventory (STAXI); - Ways of Coping with Asthma in Everyday Life (WCAEL); Illness behaviour questionnaire (IBQ)

Table 1.2. Study design and key findings: Relationships between emotional regulation strategies and asthma morbidity outcomes

SN	Design	Statistical analysis	ER strategy x outcome	Key finding: the relationship between ER strategy and primary/secondary outcomes		Quality rating*
				Baseline ER x baseline outcome	Baseline ER and outcome at F/U	
1.	CS	Partial Correlation (adjusted for severity of asthma) Outcomes: HRQoL; HCU; Asthma Control	**EA/ACCEPTANCE** Ignoring asthma (**C-EA**) Hiding asthma (**B-EA**)	• Ignoring was negatively associated with Physical HRQoL (r=-.11***). N/s correlation with neither Psychological HRQoL, HCU nor asthma control (asthma severity). • Hiding was associated with poorer asthma control (indicated by higher severity of asthma symptoms) and Physical HRQoL. N/s association with HCU.		A
			POSITIVE REAPPRAISAL Positive reappraisal	• Higher positive reappraisal score was linked with better Psychological HRQoL (r =.23***) but n/s association with neither HCU nor asthma control (symptom severity).		
			PROBLEM-SOLVING Information seeking	• More information seeking was linked to higher asthma severity (r = .27***), worse physical HRQoL (r = -19***) and higher frequency of GP and nurse visits (r =.16*** and r =.14***).		
			RUMINATION/WORRY Asthma worry	• Greater asthma worry was associated with poorer asthma control (indicated by higher asthma severity) (r=.46***), higher frequency of both GP and nurse visits (r=.08 and r=.11***) and negatively correlated with both Psychological and Physical RAND-36 scores (r = -.18*** and r = -.18***).		
2.	LT (12m F/U)	Multi-variate logistic regression (adjusted for age, sex, education, employ. and income) Outcomes: HCU	**EA/ACCEPTANCE:** Avoidance coping (**CB-EA**) Denial (**A-EA**)		• Lower avoidance scores were significantly associated with lower likelihood of asthma related hospital admissions (OR = .4, 95% CI = .3 – .6, p <.0001 strong association) and repeated admissions (>2) (OR = .2, 95% CI = .1–.5, p = .0005) at 12m F/U. • Higher avoidance was linked to repeated A&E visits (>2) at 12m F/U (OR =.6, 95% CI =.4 – .8, p = .001). • n/s correlations between denial and neither hospital admissions nor A&E visits.	A
			PROBLEM-SOLVING		• Problem solving was negatively linked with >2 A&E visits at 12m F/U (OR = .7, 95% CI = .5 – 1.0, p = .05)	
3.	Prospect. RCT (12m F/U)	ANOVA (controlled for age and gender) Outcomes: HCU	**EA/ACCEPTANCE** Denial (**A-EA**)		• (overall sample) Greater denial was associated with a higher likelihood of A&E visits (F=4.7, p=0.04) at 12m • N/s association with a number of hospitalisations.	B

4.	LT (12m F/U)	Pearson's correlation; Bivariate and multivariate longitudinal linear regression (adjusted for 1) age, gender and 2) age, gender, education, income, hospital, and baseline clinical asthma status respectively) Outcomes: HRQoL	**EA/ACCEPTANCE:** Avoidance coping Denial **(A-EA)**	Bivariate analyses (baseline scores): • Lower avoidance scores were significantly associated with a better HRQoL score on all measures. • N/s link between denial and HRQoL measures.	• Mulitvariate (baseline ER and 12m HRQoL scores): Lower avoidance scores significantly predicted higher HRQoL scores (MAQLQ; SF-36 PCS and SF-36 MCS) (β=1.20, 95% CI =.8 - 1.6; < 0.00001; β=5.5; 95% CI =2.8, 10.9; p= 0.008; β=8.0; 95% CI =2.1 - 13.9 1.9-10.5; p= 0.009 respectively). • Correlations (baseline and change scores): Lower avoidance scores correlated with improved asthma specific HRQoL scores (MAQLQ) (r= 0.49****).	**A**
			PROBLEM-SOLVING:	Bivariate analyses (baseline scores): • Greater use of problem-solving was significantly associated with higher HRQoL scores on all measures.	• Greater use of problem solving predicted better physical HRQoL scores (β=6.3; 95% CI =1.9-10.5; p= 0.004).	
5.	CS (recall at baseline for HCU 1m + 12m prior)	Partial Spearman correlation (adjusted for age) Outcomes: HCU; Asthma control	**EA/ACCEPTANCE** Denial **(A-EA)**	• N/s correlation with asthma control (indicated by symptom severity score and daily activity limitations (r=-.054 and r=0.19, both p>.5) respectively. • N/s correlation with the frequency of doctor's visits (r=-0-056, p>.05) 1 month before the asthma attack. • N/s correlation with neither the frequency of A&E visits, hospital admissions, nor ICU admissions (p>0.10) 12m before the near-fatal asthma attack.		**B**
6.	CS	Correlation Outcomes: HRQoL; Asthma Control	**EA/ACCEPTANCE:** Trait acceptance	• Greater trait acceptance was associated with greater asthma specific HRQOL (r =.37***). • N/s relationship with asthma control (r=.14, n/s).		**B**
7.	CS	Correlation Outcomes: HRQoL; Asthma Control, MC	**EA/ACCEPTANCE:** Denial	• Greater denial of asthma was associated with less intake of corticosteroids (r= N/R; p=0.015).		**B**
			POSITIVE REAPPRAISAL:	• Lesser use of a positive reappraisal was positively correlated with poorer asthma control (r=N/R; p=0.009)		
			WORRY/RUMINATION: Worry	• Greater worry was associated with poorer asthma specific HRQoL (r=-0.239; p=0.044).		
8.	CC	Stepwise regression Outcomes: MC	**EA/ACCEPTANCE:** Avoidance **(CBA EA items)**		• Avoidance was a significant predictor of medication compliance for hypertension but n/s for asthma patients.	**C**
			PROBLEM-SOLVING: Positive coping (current condition)		• N/s predictor of medication compliance.	

9.	LT (12m F/U)	Univariate Pearson's correlation and multivariate regression analysis Outcomes: HCU	**EA/ACCEPTANCE:** Acceptance Denial **(A-EA)** Distraction **(CB-EA)** **PROBLEM-SOLVING**: Planning and Active Coping **POSITIVE REAPPRAISAL:** Positive Reinterpretation **EE/SUPPRESSION:** Venting emotions (EE)		• 12m F/U: Denial was the only ER strategy that showed a positive correlation with the frequency of A&E visits (ρ = .31, p = .014). • Higher denial was positively correlated with a higher likelihood of being hospitalised due to asthma exacerbations. Results N/R for other ER strategies. • In multivariate regression: Denial was the only variable retained as a significant predictor of A&E visits (F(1, 60) = 5.53, p = .022).	**C**
10.	CS	Multivariate regression analysis (adjusted for ACT + GINA scores) Outcomes: HRQoL	**EA/ACCEPTANCE** Cognitive avoidance	• Negative association was found between cognitive avoidance (CA) and symptom component of asthma specific HRQoL (SGRQ). CA was negatively correlated with SF-36 scores (in social functioning and emotion role domains). • In the regression analysis, a greater use of cognitive avoidance predicted a poorer SF-36 scores in the emotion role (B = 16.14, p = .003; B =15.43, p = .006) but n/s predictor for Social functioning domain (B = -5.58, p = 0.22).		**A**
			PROBLEM-SOLVING: Cognitive problem coping	• N/s association between problem-solving and neither specific nor general measure of HRQoL.		
11.	CS	Spearman correlation + bivariate regression (controlled for disease characteristics, coping resources and coping style) Outcomes: HRQoL	**EA)/ACCEPTANCE** (illness specific): Avoidant coping	• N/s correlation between avoidance and HRQoL (r = -.09, p >0.10), however in regression analysis, greater avoidance scores emerged as a unique predictor of poorer HRQoL (β = .13, p = .04).		**A**
			PROBLEM-SOLVING: Rational/Problem coping style	• N/s correlation between problem solving and HRQoL for asthma patients (r = -.10, p >0.10) (but significant for COPD patients).		
12.	CS	Bivariate correlation and Hierarchic. Multiple regression Outcomes: asthma control	**EA/ACCEPTANCE:** Acceptance **EE/SUPPRESSION:** EE with labels	• N/s correlations between neither FFMQ-Nonjudgment nor FFMQ-Describing and asthma control.		**B**
13.	CS	Zero-order correlation and Regression (controlling for age, race and FFMQ subscales) Outcomes: HRQoL; asthma control	**EA/ACCEPTANCE:** Acceptance	• N/s association between Acceptance and neither asthma control (ACT) nor asthma specific QoL (AQLQ).		**B**
			EE/SUPPRESSION: EE with labels	• Greater use of expressing emotions by describing was correlated with both asthma control (ACT) and asthma HRQoL (AQLQ) (r = .33* and r = .33*). • Higher expressing of emotions by describing predicted higher AQLQ (β = .35,t = 2.46*) but not ACT scores.		

14.	CS	Direct entry linear regression (controlled for age, gender, and income) Outcomes: asthma control; HRQoL	**PROBLEM-SOLVING:** Rational PS style A constructive PS style Impulsive-careless PS style **POSITIVE REAPPRAISAL:** Positive problem orientation Negative problem orientation	• Only higher scores on the Impulsive-careless problem-solving subscale predicted both lower asthma control scores (β = .70, 95% CI = .37 – 1.04, p = .001) and lower asthma QoL (β = .79, 95% CI = .15 – 1.42, p = .017).		**B**
15.	LT (2w period)	Pearson correlation Outcomes: MC; asthma control	**EA/ACCEPTANCE:** Cognitive denial Affective denial		• Higher affective but not cognitive denial was linked with poorer medication compliance (r = –.31; p = .05). • N/s correlation between neither affective nor cognitive denial and objective measure of asthma control as indicated by lung function (FEV1%pred).	**B**
16.	CS	Spearman correlation Outcomes: HRQoL, HCU	**EA/ACCEPTANCE** Acceptance of illness	• Acceptance scores were positively correlated with physical, environmental and social relationship domain of WHQQoL (r =.67***, r = .68*** and r =.68*** respectively). • Lower acceptance scores were associated with higher HCU in the following areas: number of hospitalisation in the past 3y (r = -.44***), health care utilisation index (-.34***), number of home visits (-.30***), number of phone consultations (-.21**) and district nurse interventions (r = -.28***).		**A**
17.	CS - EMA procedure – multiple time points across 1w)	Hierarchical linear regression Outcomes: asthma control	**EA/ACCEPTANCE:** Mental disengagement (C-EA) Behavioural disengagement Denial (A-EA)		• Mental disengagement was n/s associated with neither asthma symptoms [F(1,1944) = 1.16) nor PEFR [F(1,187) = 0.64). • Greater use of behavioural disengagement predicted worse control of asthma symptoms [F(1,1944) = 6.77*] and worse control in terms of lung function (PEFR scores) - however this link was n/s [F(1,1878) = 2.64 (p<.10)]. • Greater denial scores predicted more self-reported asthma symptoms [F(1,1911)= 8.84*] and worse PEFR [F(1,1847) = 7.25*].	**B**
18.	CS - EMA procedure- 5 x daily for 1w	Correlation Outcomes: asthma control	**EE/SUPPRESSION:** Anger expression Anger suppression	• Greater Anger suppression was associated with poorer asthma control (higher asthma symptoms severity (r = .23*) and more physical limitations due to asthma symptoms (r = .28*). • N/s between Anger expression and asthma control.		**A**

*>.05; >**.01; ***≥.001;****>.0001; CS=cross-sectional; LT=Longitudinal; RCT=Randomised Controlled Trial; CC=Case Control, w= weeks, m=months; EA=experiential avoidance; C=Cognitive; B=Behavioural; A=Affective; F/U=Follow Up; EE=Emotion Expression; SN=Study Number

The relationship between emotion regulation (ER) and asthma morbidity outcomes

The following section will examine the relationship between selected ER strategies (experiential avoidance/acceptance, problem-solving, positive reappraisal, rumination/worry, and emotion expression/suppression) and asthma morbidity outcomes.

Emotion regulation and indicators of asthma control

Out of the 10 studies which measured asthma control four used standardised asthma control measures [S6, 12, 13,14], four included self-report scales (frequency/severity of symptoms) [S1,5,17,18] and two employed objective measure of asthma control (e.g. PEFR and FEV1%predicted) [S15,17]. The most frequently used validated questionnaires to measure asthma control were Asthma control questionnaire (ACQ) [51,53] (2 studies) [S6,14] and Asthma Control Test (ACT) [69] (2 studies) [S12,13].

Avoidance/Acceptance

Three studies [S6,12,13] assessed the role of acceptance in asthma control. Two studies measured acceptance using the non-judgement subscale of the Five Facet Mindfulness Questionnaire (FFMQ) [67] [S12, 13] and one study used the Child and Adolescent Mindfulness Measure (CAMM) [51] [S6]. All three studies used a validated self-report questionnaire to assess asthma control with two studies utilising Asthma Control Test (ACT) [69] [S12, 13] and one study using the Asthma Control Questionnaire (ACQ) [53]. All three studies showed that acceptance was not significantly associated with asthma control.

All three studies were of satisfactory methodological quality with two studies [S12, 13] being limited by employing relatively small samples (n = 56, n = 61) respectively. Study 12 but not 13 was calculated to have enough statistical power, but a larger sample would increase confidence in findings. Studies 13 and 6 were limited by using a non-representative non-smoking community sample [S13] and school/college students of particular asthma severity (excluding milder cases not taking preventative medication) [S6]. The studies also varied in the levels of asthma control represented by mean scores ranging from well-controlled [S12], borderline adequately controlled [S6]

and poorly controlled [S12]. This makes it difficult to conclude findings across different asthma settings and different levels of asthma control.

Four studies [S1,5,15,17] looked at the relationship between avoidance and asthma control. Three of these studies focused on cognitive avoidance (including cognitive denial and mental disengagement) [S1,17,15], three on affective avoidance (e.g. denial) [S5,15,17] and two studies [S17,1] included subscales focused on mostly behavioural avoidance. All three studies found that cognitive avoidance was not significantly associated with indicators of asthma control measured by self-report severity of symptom scale [S1], objective measure of lung function (FEV1%predicted and PEFR) [S15,17] and electronic momentary assessment of asthma symptoms [S17].

With regards to behavioural avoidance, study 1 found that hiding asthma from others was positively associated with poorer asthma control (indicated by higher severity of asthma symptoms). In study 17, although greater use of behavioural disengagement predicted poorer asthma control in terms of higher severity of symptoms and worse lung function (PEFR scores), this link did not reach significance. This study was limited by the non-representativeness of the recruited population and by not accounting for confounding variables. Although it employed a sample size which had enough power (n =61), a larger sample size would increase confidence in the findings.

Studies exploring affective avoidance mainly focused on the relationship between denial and asthma control [S5, 15, 17]. One study [S17] found that a greater tendency to employ denial as an emotion regulation strategy was significantly associated with poorer asthma control as indicated by higher asthma symptom severity and poorer lung function. A different result was found by two studies [S5, 15] which found a non-significant correlation between affective denial and asthma control as measured by lung function (FEV%pred) [S15] and asthma severity score [S5]. All three studies were of satisfactory methodological quality. Limitation of study 17 has been described above. Study 15 was limited by a non-representative sample and not controlling for confounding variables. Study 5 was limited by employing small sample size with insufficient power using a non-validated measure of asthma severity.

Problem-solving

Two studies explored problem-solving and asthma control [S1,14]. Both studies found a significant association between greater problem solving and asthma control. However, the direction of this relationship differed across studies. Study 1 found that greater use

of problem-solving (strategy of information seeking) was significantly linked to poorer asthma control (indicated by higher reported severity of asthma symptoms). Study 14 found that greater application of impulsive, careless and hurried problem-solving skills has been associated with poorer asthma control scores.

Worry Rumination

Only one study looked at Worry/Rumination and asthma control [S1]. This study found that greater asthma worry was strongly associated with poorer asthma control (indicated by higher asthma severity) in a sample of hospital outpatients with asthma. This was a good quality study with a very large sample drawn from the general population.

Emotion Expression/Suppression

Three studies looked at the relationship between the use of emotion expression/suppression and indicators of asthma control. Only one study explored emotion suppression [S18]. This study found that suppressing emotions (anger) was associated with poorer control of asthma symptoms as indicated by both higher asthma symptoms severity and more physical limitation due to asthma symptoms. This study was of good methodological quality. Of note is the high proportion of female participants (72%) in the study.

Three studies looking at emotion expression found that expression of negative emotions (anger) [S18] was not significantly linked to indicators of asthma control (asthma severity, function limitation). There were mixed results with regards to a relationship between general emotion expression (through labelling) and asthma control [S12,13]. Whilst study 13 reported a significant positive relationship with asthma control scores, study 12 noted n/s association. Both studies used the same measure of emotion expression (FFMQ) and asthma control (ACT).

The discrepancy in results might be due to several methodological differences. Study 12 included a younger population of Psychology undergraduate students whilst study 13 was conducted in a community sample of adults with asthma with a higher mean age. Both studies were of satisfactory methodological quality, both limited by relatively low sample size. Study 12 was limited by not adjusting for potential covariates whilst study 13 used sample with limited representativeness to the target population. The two samples also varied in levels of asthma control. Whilst the student sample reported well-controlled asthma, the community sample had mean asthma

control scores within the poorly controlled range. It is likely that individuals with well-controlled asthma experience less asthma-related stressors and might have fewer opportunities or need to regulate their emotions through expression. Since Undergraduate Psychology students by nature are likely to be a relatively homogenous group and have more developed skills in and value expressing emotions, findings from this study are not generalisable to the wider asthma population.

Positive reappraisal

Three studies explored whether individuals' tendencies to regulate their emotions by positively reappraising stressful situations are linked with asthma control. Two of these studies found that positive reappraisal was not significantly correlated with indicators of asthma control as measured by asthma severity scale [S1] and Asthma Control Questionnaire (ACQ) [S14]. To strengthen these findings, negative appraisal, which can be viewed as the opposite end of the appraisal continuum, was also not significantly correlated with asthma control scores [S14]. A different pattern was reported by [S7] who found that less use of positive reappraisal was linked with poorer asthma control scores (ACQ).

The two studies were both of satisfactory methodological quality. Study 1 included a very large sample size (n = 3496) and a representative sample drawn from a general population of adults with asthma. However, it employed a non-validated self-rated scale to measure the severity of asthma symptoms as indicators of asthma control. Study 14 showed some methodological limitations such as inadequate sample size (n = 44) and less representative sample (excluding milder cases of adults with asthma who did not report asthma medication use). These studies also varied in terms of asthma context. Study 1 recruiting participants from the general population with a mean asthma control of the sample indicative of mild (well-controlled asthma). Whilst the sample recruited by study 14 and study 7 were drawn from the same data set and included hospital outpatients with higher asthma severity.

Therefore, the evidence from study 1 carries higher weight and increases confidence in the above findings. However more well powered and representative studies using the same indicators of asthma control are needed to replicate these findings.

Emotion regulation and health-related quality of life (HRQoL)

Seven out of nine studies looking at HRQol employed asthma specific HRQoL measures. Only 2 studies employed the same instruments to measure HRQoL, namely mini Asthma Quality of Life Questionnaire (AQLQ) (asthma specific measure) [56] [S7,14] and Short-Form Health Survey (SF-36) (general measure) [48] [S4,10].

Avoidance

Four studies explored the relationship between avoidance and HRQoL [S1,4,10,11] with two studies exploring multiple aspects of avoidance [S1,4]. Four studies which employed subscales focusing on a cognitive-behavioural aspect of avoidance found that it was linked to poorer asthma HRQoL outcomes [S1,4,10,11]. This was the case for both asthma specific [S4,11] and general aspects of HRQoL [S4,10,1].

All three studies were of good to satisfactory methodological quality and employed relatively large sample sizes with a study 1 employing a notable sample size of 3496 participants. One of these studies focused on general population [S1], one included primary care patients with milder asthma severity [S11], whilst the remaining two explored hospital outpatient population with higher asthma severity [S4,10]. This suggests that the impact of avoidance on HRQoL might not necessarily be influenced by the severity of asthma. One study which focused on denial, an affective dimension of avoidance found that this style of ER was not significantly associated with neither asthma specific nor general HRQoL [S4].

Problem-Solving

Five studies looked at problem-solving and HRQOL [S1,4,10,11,14]. Two studies found a positive relationship between greater use of problem-solving and a better asthma specific [S4,14] and general HRQOL [S4], whilst one study [S1] found that greater problem-solving was linked with poorer Physical domain of HRQoL. Study 1 and 4 looked specifically at information seeking and information seeking and planning respectively. In study 4, baseline PS scores were linked to a better HRQoL on both asthma specific and general measures at baseline. However, this association remained significant only for the physical aspect of general HRQoL at 12month F/U.

In contrast, two studies [S10,11] found no significant relationship between problem-solving and HRQoL. Both studies [S10,11] employed relatively large samples

and were of satisfactory methodological quality. However, compared to other studies, study 11 used a sample of primary care asthma population characterized by less severe asthma. It is also important to note that a high proportion of a recruited population (66%) in study 10 reported well-controlled asthma. It is possible that a population with less severe and better-controlled asthma, are exposed to less asthma-related stressors and experience less negative affect. These individuals might have less need or opportunities to employ problem-solving skills to regulate difficult emotions. Another reason for the disparity in findings across studies could be due to different aspects of problem-solving measured. Whilst study 1 and 4 specifically focused on information seeking aspect of problem-solving, study 10 and 11 included more general problem-solving measures.

Rumination/Worry

Only two studies explored the emotion regulation strategy of worry with HRQoL in asthma patients. Both studies found that the tendency to employ worry to cope with difficult emotions was linked to poorer asthma specific [S7] and general HRQoL [S1]. These studies were of good [S1] and satisfactory methodological quality [S7].

Positive reappraisal

Only one study explored positive reappraisal and HRQoL and found that, amongst the general asthmatic population, greater use of positive reappraisal was associated with better general HRQoL [S1]. This was a good quality study with a large sample.

Emotion suppression/expression

Only one study [S12] explored the relationship between emotion expression and HRQoL. It reported that in the community sample of adults, greater use of expressing emotions by describing was associated with better asthma specific HRQoL (higher AQLQ scores). This study was of satisfactory methodological quality, limiting its sample representativeness by excluding smokers and having a small sample size. Its relative strength was controlling for age, race and other FFMQ subscales.

Emotion regulation and health care utilisation (HCU)

A total of 6 studies assessed ER and indicators of health care utilisation (HCU) [S1,2,3,5,9,16].

Avoidance/Acceptance

One identified study [S9] looked at the relationship between acceptance and HCU. It found that lower acceptance scores were associated with a higher number of hospitalisations in the past 3y, HCU index, home visits, phone consultations and district nurse interventions. Acceptance was not significantly associated with a frequency of A&E visits.

Five studies explored avoidance [S1,2,3,5,9]. Three studies explored the use of general avoidance as a strategy to regulate emotions (cognitive and behavioural elements) [S1,2,9] and 4 specifically looked at the use of denial [S2,3,5,9].

Two out of the three studies looking at general avoidance strategies found that neither were significantly associated with indicators of HCU. In study 9 the strategy of distraction at baseline was not significantly associated with the frequency of self-reported A&E visits in the past 12 months. Other avoidance strategies of hiding and ignoring were also not significantly associated with HCU, specifically with asthma-related GP and nurse visits in the past 12 months [S1].

Different results were reported by study 2, which found that those who used less avoidance at baseline were less likely to be admitted to hospital due to asthma, have less repeated hospital admissions (defined as having more than 2) and less repeated A&E admissions at 12 months follow up. Compared to study 9, which employed hospital outpatients, study 2 employed a population with higher asthma severity and used a sample of both hospital outpatients and inpatients including those attending A&E. Study 2 also recruited subjects with respiratory and other comorbidities, whilst these were excluded from study 9. These methodological disparities might account for the different finding regarding A&E visits.

Three of the studies looking at denial and HCU employed longitudinal design and looked at denial at baseline and indicators of HCU at 12 months F/U [S2,3,9]. One study was cross-sectional and looked at baseline denial and baseline recall of HCU 1 months and 12 months before a near-fatal asthma attack [S5]. Four studies [S2,3,5,9] looking at A&E visits reported mixed findings. Study 3 and 9 found that denial at baseline was

associated with A&E visits at 12 months follow up. Denial was not associated with A&E visits in 2 studies [S2, 5].

Three out of 4 studies looking at denial and hospitalisations, found a non-significant link [S2,3,5], whilst study 9 found a positive correlation. Study 5 found a non-significant relationship between denial and ICU admissions 12 months before near-fatal asthma attack and between denial and doctor's visits 1 month before near-fatal asthma attack.

In addition to some of the methodological aspects described above, some disparities in findings might be due to differences in the denial measures employed. Study 2,3 and 5 employed the same measure of denial, namely Illness Behaviour Questionnaire (IBQ) [39], whilst study 9 employed the denial subscale of COPE [38]. Study 2 and 5 both employed samples with patients with severe asthma whilst 3 and 9 included sample with moderate and moderate to severe respectively. Study 2, 3 and 5 were all conducted in Australian's teaching hospitals with study 2 and 3 conducted by the same research group and study 3 and 5 being conducted in the same hospital. Study 9 was conducted in Spain which might present a difference with regards to cultural and contextual factors. Study 9 also employed hospital outpatient sample only, compared to study 2,3 and 5 which recruited their samples from both outpatient and inpatient hospital settings and study 2 and 5 also including those presenting at A&E. Study 5 employed those who presented at A&E with nearly fatal asthma attack which might present individuals with a unique life stressor compared to the remaining studies. Study 2 was of good methodological quality. Study 3 and 5 were rated as satisfactory with regards to a risk of bias, whilst study 9 was rated as being of poor methodological quality.

Problem-Solving

Two studies explored the relationship between problem-solving and HCU [S1,2]. Both studies found that problem-solving was associated with higher HCU. However, the direction of this relationship differed. Whilst in study 2, greater baseline problem-solving score was correlated with less GP and nurse visits [1] less repeated (>2) A&E visits at 12 months F/U, study 1 found that greater problem solving (information-seeking strategy) was linked with higher HCU in the past year. Both studies were of good methodological quality. Due to the cross-sectional nature of study 1, which makes it difficult to identify the direction of the relationship that the results might also mean that individuals who utilise health care more might be seeking more information.

Rumination/Worry

In one good quality study [S1], greater asthma worry was associated with a higher frequency of both GP and nurse visits in the past 12 months.

Positive reappraisal

Two studies explored whether positive reappraisal is associated with HCU [S1,9]. Both studies found a non-significant relationship between positive reappraisal and HCU, specifically the frequency of GP and nurse visits [S1] and A&E visits [S9] in the past year.

Emotion suppression/expression

The only identified study [S9] which explored emotion expression, found that it was not significantly associated with HCU, namely frequency of A&E visits at 12 months follow up. This study was of poor methodological quality, limited by the representativeness of the recruited population, inadequate power, and lack of adjustment for confounding variables.

Emotion Regulation and Medication adherence

Avoidance

Three studies explored the relationship between avoidance and medication adherence [S7,8,15]. One study (S8) focused on general avoidance (cognitive, behavioural and affective components), whilst two focused on affective avoidance, specifically the strategy of denial.

Both studies found that greater use of denial was significantly associated with poorer adherence with asthma medication [S7,15]. However, in S15 this was only the case for affective denial and not cognitive denial. Although the association between cognitive denial and medication adherence did not reach significance, it was reported that individuals in the suboptimal compliance group had significantly higher total cognitive denial scores. Studies differed in the type of medication explored. In study 7 authors looked at adherence with prescribed corticosteroids whilst study 15 used an objective micro-electronic monitor to measure compliance with inhaled controller medication (non-specified). Both studies [S7,15] were of satisfactory methodological quality. Study 15 was limited by insufficient power, but its relative strength was

employing an objective measure of adherence which introduces less bias due to poor recall of symptoms. More studies with adequately powered samples are needed to see whether the non-significant result for cognitive denial was influenced by a lack of power and to gain more trust in findings regarding the affective denial.

Study 8 found a non-significant relationship between general avoidance and medication adherence in asthma patients. This study included a wider range of controller medication such as theophylline, corticosteroids, beta-antagonists and other preventative agents). In study 8, asthmatic patients reported experiencing a high level of medication side effects and these have emerged as a unique significant predictor of compliance in regression analysis. It is possible that when medication side effects are prevalent, these might take precedence as a variable predicting poor compliance over denial. However, this study was of poor methodological quality and findings were based on a limited number of participants (n = 14).

4. Discussion

This was a broad systematic review aimed at exploring how the emotion regulation strategies utilised by adults with asthma influence their asthma morbidity outcomes. Specifically, it focused on the following outcomes: HQoL, health care utilisation, medication adherence and markers of asthma control. As previously highlighted the research into the relationship between emotion regulation strategies and the selected asthma morbidity indicators has been lacking. This was evident by the limited number of studies retained in the current review which looked at each strategy and outcome of interest. Those studies included often shared common methodological limitations such as representativeness (10/18 studies) of included samples, failure to explore potential confounding factors and to include these in analyses (8/18 studies) and lack of power (7/18 studies).

Taking into consideration the methodological limitations, the current systematic review highlighted several interesting findings.

The relationship between emotion regulation strategies and asthma morbidity outcomes.

The review highlighted significant relationships between emotion regulations strategies viewed in the literature as adaptive (acceptance, positive appraisal, emotion expression) and better asthma morbidity outcomes. It also found that greater use of strategies previously described as maladaptive (avoidance, emotion suppression and worry) was linked with poorer asthma outcomes. The role of these depended on the specific emotion regulation strategy and morbidity outcome studied.

Emotion regulation strategies associated with poorer asthma morbidity outcomes

The results from the review provided some preliminary evidence that increased use of avoidance and worry as strategies to regulate difficult emotions were associated with poorer HRQoL in adults with asthma. This evidence was based on studies of good to a satisfactory quality.

Avoidance was consistently related to HRQoL across all included studies (n =4) with samples drawn from a variety of asthma settings suggesting that it might be a factor influencing HRQoL despite someone's severity of asthma symptoms. The findings are

specific to the cognitive and behavioural aspects of avoidance and are in line with research from other chronic illnesses such as cancer [83-85].

The findings regarding worry and HRQoL are in line with research studies in other chronic health conditions such as diabetes and cancer which showed that increased illness worry was linked with poorer HRQoL [85]. Previous evidence suggested that using worry to regulate emotions might result in individuals getting enmeshed with difficult emotions, which further increases their duration and intensity [86]. This is likely to influence their adjustment to illness and quality of life [86-87]. Evidence for the association of worry and HRQoL were based on a small number of studies (n=2). Although these were of good to satisfactory methodological quality, more studies are needed to confirm these findings.

The systematic review highlighted that greater use of avoidance, suppression of negative emotions and worry showed most consistent associations with poorer indicators of asthma control (higher severity of symptoms and physical limitations due to symptoms).

This evidence is specific to the use of behavioural avoidance and was based on a limited number of studies (n=2). Cognitive avoidance was consistently non-significantly associated with asthma control and evidence regarding the role of denial showed mixed results. The role of worry was based on one methodologically strong study. These findings are also consistent with extensive research showing that avoidant behaviour and worry negatively influences illness control in the chronic population [88-89].

The findings are also in line with an extensive body of previous research which suggests that the suppression of negative emotions including anger have been connected with poorer physical health across chronic illness population with coronary heart disease, rheumatoid arthritis and cancer [90-92]. One explanation is the lingering nature of suppressed emotions which can build up over time and resurface with higher intensity. The continuous suppressing efforts can then deplete self-regulatory processes needed to engage in other tasks such as self-management and engagement with valued activities [93].

The role of positive appraisal showed mixed findings and more studies with higher methodological quality are needed to replicate findings using consistent asthma control measures.

Some preliminary evidence suggests that avoidance, specifically affective avoidance strategies such as denial were linked with poorer adherence with asthma

medication. However, only a small number of studies explored this relationship (n=3) and more studies are needed to confirm these findings. The evidence between denial and medication adherence is in line with research looking at patients with cardiovascular disease and HIV [94-95].

People with the tendency to employ denial are likely to minimise the seriousness of their asthma and be less aware of associated risks to their well-being. This is likely to influence their motivation to comply with medication regimens to manage their illness [95]. Some preliminary evidence from this review showed that affective rather than cognitive elements of denial are associated with poorer medication adherence. It might be that an individual's tendency to deny emotional experiences such as anxiety might be a more important factor in adherence as some level of for example anxiety can aid motivation to engage in health behaviours.

Overall, avoidance was the only emotion regulation strategy studied with regards to medication adherence. Given the importance that compliance with asthma medication has on asthma outcomes such as quality of life, HCU and asthma control, further research should emphasise exploring its correlates. Future studies would benefit from more consistent operationalization of denial.

Preliminary results from one good quality study suggest that greater asthma worry is linked with higher HCU, specifically higher frequency of both GP and nurse visits in the past 12 months. This is consistent with previous research on illness worry and HCU [e.g. 96]. More studies are needed to confirm these findings.

ER associated with better asthma morbidity outcomes

The systematic review showed some preliminary evidence that greater use of, positive reappraisal, emotion expression by describing and acceptance were linked to better HRQoL scores. Emotion expression was linked to better asthma control.

The findings regarding the adaptive role of positive reappraisal in HRQoL are consistent with previous research in both healthy and chronically ill population which linked reappraisal with better physical and psychological wellbeing [92,97]. Previous research suggested that positive reappraisal is likely to influence HRQoL by decreasing the negative impact of difficult emotions [98].

The findings are also consistent with previous evidence which found that emotion expression by describing was correlated with HRQoL and asthma control in both general and chronic health population [99-101].

It was suggested that those who can describe their emotions are more likely to have an increased understanding of their emotional experiences and be able to effectively communicate these to others [68]. This can lessen the emotional intensity of these experiences and their potential to drive unhelpful behaviour which can negatively influence both HRQoL and asthma control [102]. It is also possible that those who can identify and describe their emotions to others more readily have a higher chance of receiving more social and health care support and getting their needs met. This is likely to positively impact on their well-being and symptom control.

However, the evidence for both positive appraisal and emotion expression was based on only one study for each asthma outcome and more evidence is needed regarding these factors in asthma population.

Some preliminary findings regarding the positive role of acceptance on HRQoL (n=3) were consistent with previous evidence suggesting that acceptance skills might positively influence once well-being through non-judgmentally appraising the impact of their asthma symptoms on daily life [103].

It was also previously suggested that although acceptance influences appraisal of symptoms it is less orientated towards goal-directed behavioural change. As such it is less likely to influence actual self-management behaviours and physical symptoms [103]. This might explain why acceptance has previously been shown to correlate with HQoL but not asthma control of symptoms [103]. This was also the pattern found in the current systematic review where acceptance was consistently non-significantly associated with asthma control. This evidence for acceptance included consistent outcome measures of asthma control (ACT/ACQ), which allowed for a better comparison of findings

We have found non-conclusive results regarding a relationship between problem-solving and HRQoL, with a mixture of positively (n=2) negatively (n=1) and non-significantly (n=2) correlates studies. Studies explored different aspects of problem-solving and used a variety of measures which made it difficult to summarise findings.

Neither Positive reappraisal nor emotion expression was found to be significantly correlated with HCU**.** Given the small number of studies, the poor methodological

quality of the majority of these, and the fact that different HCU indicators were measured for positive reappraisal, conclusions cannot be made regarding these associations.

Limitations and future direction

The results from the current systematic review need to be considered in light of several limitations. Due to a lack of access to translation resources, only articles published in English and Czech were considered for inclusion in this review. Since no eligible studies were identified in Czech, this review relied solely on studies published in English.

Although the current systematic review applied specific criteria regarding the inclusion of specific emotion regulation strategies based on previous research (e.g. 30), given the review's complexity and overlapping nature of some constructs, a degree of selection bias might have potentially been introduced. The decision to combine emotion regulation strategies and coping strategies could also be regarded as a limitation as these might differ slightly in the way they are conceptualised. However, at the strategy level, both concepts measure how individuals consciously employ efforts to regulate difficult emotions, which was the focus of this review. Conducting a broad emotion regulation review has advantages of highlighting universal patterns across the available evidence base.

The variability of measures identified within the current review highlighted that future research would benefit from a better operationalisation of emotion regulation strategies and consistency in employed measures. This would enable better comparison of findings across studies.

Due to the limited research looking at emotion regulation strategies and asthma outcomes in adults, the current review included studies with a wide range of study designs, measurement tools and a heterogenous asthma population with different disease severity in various asthma settings. These individuals are likely to face different asthma specific challenges and experience different frequency and intensity of situational stressors. These are factors which are likely to impact on individuals' emotional responses and the type of emotion regulation strategies they will use to manage these. This has made it more difficult to compare findings across studies. However, there are many challenges which asthma individuals have in common such as on-going strain related to self-management regimens, increased risk of psychological difficulties such

as anxiety and low mood, daily restrictions and experience of unpleasant and often unpredictable asthma symptoms [2,5].

Majority of included studies did not consider physical and psychological comorbidities which are common in clinical practice and likely to influence both emotion regulation and asthma outcomes. These methodological issues were likely to limit the internal and external validity of the studies and influence review findings. It was previously suggested that individuals with anxiety and low mood often have attention and cognitive biases towards more threatening and negative information in their environment [104]. These biases can make it more difficult to employ some of the emotion regulations strategies such as positive reappraisal which requires individuals to shift their attention to more positive information in their environment and/or evaluate events in a more positive light. Similarly, individuals with anxiety and low mood might have a lower self-regulatory capacity to employ more cognitively focused strategies such as problem-solving [105]. Therefore, future studies should assess how these co-morbidities influence the use of specific emotion regulation strategies and their impact on asthma outcomes.

The current systematic review employed a modified quality assessment tool to assess the methodological quality of the included studies, which has not previously been validated. This can limit the reliability and validity of quality appraisal. However, the checklist was based on a Downs and Black's checklist [34] which has previously shown to be a valid and reliable tool to utilise in systematic reviews [34, 106]. A proportion of the full-text articles were rated by a second reviewer, with inter-rater checks producing a high degree of agreement. This was likely to strengthen the reliability and validity of the methodological quality ratings by reducing subjective rating bias.

Due to the cross-sectional nature of many included studies, causal inferences could not be made about the found associations between emotion regulations strategies and asthma outcomes. For the same reason, the direction of these relationships could not be determined. For example, a more effective emotion regulation skills might result in better HrQoL, but it might also be that a better HQoL might make it more likely for someone to employ more effective regulation skills.

The current review was also limited by a small number of studies included for each combination of emotion regulation strategy and asthma morbidity outcome.

Further studies should address methodological limitations highlighted in this review and employ longitudinal design to help clarify the direction of reported associations.

Clinical Implications

The current systematic review highlighted those specific strategies which were linked with better asthma morbidity outcomes. It also suggested that certain strategies might be more beneficial when considering different asthma outcomes. This might inform the design and tailoring of psychological interventions to support adults with asthma who have difficulties regulating their emotions. In particular, acceptance-based interventions such as the ACT or Mindfulness-based interventions might be beneficial to foster better HRQoL, whilst interventions such as CBT might help individuals with asthma to learn skills in cognitively appraising their problems, learn skills to cope with worry and target avoidance, to improve their asthma control, HCU and medication adherence [107-108]. However, further research is needed to evaluate these interventions in asthma patients, focusing on specific emotion regulation strategies and asthma morbidity outcomes. Creating asthma services which highlight emotional experiences as a crucial part of asthma care can reduce some stigma regarding the expression of emotions. Clinicians modelling or encouraging emotion expression might benefit patients who tend to control or suppress their emotions. Most psychological interventions focus on helping individuals to increase awareness of their emotions and support them to learn skills in expressing and labelling their experiences. This can improve outcomes in patients with asthma in terms of their health outcomes. Educating families of patients with asthma about the importance of fostering emotion expression might also enable them to better support their loved ones [109].

Conclusion

Findings from the current review highlighted that psychological interventions aimed at promoting more adaptive emotion regulation skills in adults with asthma might positively influence their asthma morbidity outcomes. Further research is needed, using improved methodological design and a clearer conceptualisation of emotion regulation construct.

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Chapter 2: Empirical paper

The role of generalised anxiety in asthma morbidity: Experiential avoidance and self-efficacy as mediators

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Abstract

Objective: Although generalised anxiety (GA) has a substantial influence on asthma outcomes, the underlying mechanisms remain unclear. This study examined individuals' Self-efficacy (SE) to manage asthma and tendency to avoid unpleasant internal states (Experiential Avoidance) (EA) as potential mechanisms that mediate the relationship between GA and asthma outcomes: Asthma Quality of Life (QoL), Asthma Control and Short-acting asthma reliever medication (SAARM) use. ***Methods:*** Data were obtained from the NHS Outpatient Respiratory clinic setting and included 65 adults with asthma. Path analysis was used to examine mediating effects. ***Results:*** After controlling for covariates, it was found that both SE to control asthma and EA mediated the relationship between GA and both asthma control and asthma QoL. Neither SE to control asthma or EA played a mediatory role in the relationship between GA and SAARM. ***Conclusions:*** The results provide preliminary support for the use of psychological interventions targeting individuals' SE to control their asthma and EA to improve asthma control and QoL in adults with asthma and co-morbid GA.

Keywords: generalised anxiety; experiential avoidance; self-efficacy; asthma; quality of life; asthma control

1. Background

Asthma is a long-term health condition which is caused by obstruction of the airways due to inflammation [1]. Even though asthma symptoms can be managed very successfully through self-management and medication, it is estimated that in the UK around 1200 people a year die because of asthma [2] and more than 50% live with asthma which is poorly controlled [3]. Poor asthma control in adults was associated with worse outcomes with regards to mortality, asthma-related quality of life (QoL) and higher utilization of health care services [3]. This highlights the need for a better understanding of factors that hinder effective asthma control and QoL to reduce unnecessary asthma-related personal/economic burden and mortality.

In recent years it has become apparent that psychological factors can explain an important proportion of variance in asthma outcomes [4,5]. Generalised anxiety (anxiety characterized by the presence of unspecified, frequent and uncontrollable worries) (GA) has shown to be particularly prevalent in this population compared to individuals without asthma diagnosis [6,7]. Higher levels of GA have been linked to poorer asthma outcomes such as asthma control, diminished asthma-related QoL and higher use of health care utilization [4,8,6].

Despite the evidence that GA can lead to poorer asthma outcomes, less is known in the literature about the underlying mechanism which can explain this relationship. One proposed pathway for the potential effect of psychological factors such as anxiety on asthma outcomes is through its effects on self-management and health behaviours [9]. Two psychological mechanisms which warrant more investigation include experiential avoidance (EA) and self-efficacy (SE). These concepts are commonly reported in subjects with high anxiety and have previously been linked to poorer health outcomes and self-management behaviours. Looking at psychological mechanisms is advantageous as these are amendable through simple psychological interventions.

EA is emotion regulation style defined by a tendency to control or avoid unpleasant internal experiences (including feelings, thoughts and physical sensations [10]. It was previously indicated that individuals with GA have a lower ability to regulate unpleasant internal experiences and are more likely to engage in EA [11-13]. EA has shown to be associated with poorer self-management behaviours such as medication compliance and poorer disease control in chronic illnesses such as HIV and diabetes [14,15]. Avoidance of internal experiences has also been repeatedly associated with worse well-being and QoL in chronic health population [e.g. 16, 17].

One proposed mechanism in the literature suggests that in individuals with anxiety, EA leads to an increase in the frequency and intensity of suppressed internal experiences and their emotional, cognitive and physiological impact [18-20]. A prolonged effort and focus on avoiding and controlling negative internal experiences are likely to lead to a depleted cognitive, attentional and emotional resources which are needed to successfully self-manage illness and make appropriate behavioural choices [21].

Self-management behaviours in asthma might also trigger distressing illness-related thoughts and feelings for patients. In individuals with higher EA, this might

result in the avoidance of self-management regiments or the use of unhelpful short term relieve strategies [22,23]. Previous research showed that psychological interventions targeting EA led to an improvement of self-care in other chronic health conditions such as diabetes [24,25].

This suggests that affective regulatory processes such as EA should be considered as an important factor influencing the relationship between distress and health outcomes. Despite this evidence, no published study to date has explored whether high levels of EA avoidance influence the relationship between levels of GA and asthma outcomes. Also, a large body of existing evidence looking at EA in other chronic health population has been limited by employing the Acceptance and Commitment Questionnaire (AAQ-I) [17] and revised AAQ-II, [26] widely criticised for its poor psychometric properties and discriminant validity [27-29]. Further investigations using an alternative measure of EA is warranted to confirm previous findings.

Another important factor that may also partially explain the link between anxiety and asthma-related outcomes is the individual's perceived ability to manage their asthma, construct known as self-efficacy (SE) [30]. In individuals with asthma, co-morbid anxiety might reduce their confidence and perceived control over their symptoms, negatively influencing their SE to self-manage their asthma. Indeed, a previous study by Lavoie et al. [6] found that amongst individuals with asthma, higher levels of GA were associated with lower self-reported asthma-related SE. Asthma-specific SE is then a well-established factor associated with worse overall asthma control, greater frequency of using a short-acting reliever medication and poorer asthma-related QoL [6, 31-34]. However, to date, there is a lack of understanding in the literature regarding SE as a potential factor influencing the relationship between GA and poor asthma morbidity.

The current study was conducted to address some of the gaps in the previous research literature by investigating the relationship between GA and asthma morbidity indicators (asthma control, use of reliever asthma medication, asthma QoL) in adults with asthma and whether individuals' SE and EA mediate this relationship. The current study also tried to address previous methodological limitations by employing more recently developed Brief Experiential Avoidance Questionnaire (BEAQ) [10] as a measure of EA. This measure has shown good psychometrics and thus might represent a more suitable measure to address AAQ limitations.

We hypothesise that:

(1) In adults with asthma, higher levels of generalised anxiety (GA) will be associated with
    a) poorer asthma morbidity indicators (asthma control, use of reliever asthma medication and asthma quality life),
    b) lower Self-efficacy to manage asthma and
    c) greater Experiential Avoidance.

(2) In adults with asthma Self-efficacy (SE) and Experiential Avoidance (EA) will mediate the relationship between:
    a) generalised anxiety and asthma control
    b) generalised anxiety and the use of reliever asthma medication and
    c) generalised anxiety and asthma quality life.

The project intends to benefit clinical practice by increasing our current understanding about psychological mechanisms which can potentially be targeted to improve asthma outcomes such as asthma control and asthma QoL. More comprehensive interventions will directly benefit NHS by reducing costs associated with poorly controlled asthma and by alleviating personal burden for individuals with asthma.

2. Methods

2.1. Participants

Participants were recruited consecutively from the respiratory outpatient hospital clinics at NHS Fife and NHS Greater Glasgow and Clyde if they met the following inclusion criteria: age 16 – 75 years, confirmed diagnosis of asthma without other illness presenting higher morbidity, treated for asthma for at least the last 6 months, good written and spoken understanding of English language. Patients were made aware by screening clinicians as well as in the patient information sheet that they are not eligible to take part in the study if they self-report to currently experience episode of serious mental illness such as psychosis, currently misusing alcohol or drugs or having a diagnosis of fibromyalgia. An acute episode of psychosis, as well as on-going substance misuse, were excluded due to its potential confounding influence on the perception of symptoms, recall of information as well as self-management behaviours. Participants were made aware by screening clinicians as well as in the study information sheet that they can still participate in the study before the end of the study date if their situation changes. Comorbid fibromyalgia in adults with asthma can lead to reduced cardiorespiratory fitness, altered perception of airway obstruction and increased hyperventilation [34b]. Therefore, in this study adults with asthma with co-morbid fibromyalgia were not eligible to take part to account for its potential confounding influence on the severity of respiratory symptoms unrelated to asthma disease.

2.2. Power and sample size

The calculation of a sample size needed to detect conditional indirect effects in mediation analyses is complex and research into this has been lacking [35]. Per recommendations by Fritz & MacKinnon [36], it has been estimated that for mediation analyses a sample size of 71 will achieve a power of .8 to detect a medium effect size of the indirect effect.

2.3. Procedure

The study received NHS Ethical approval from the Yorkshire & The Humber - Leeds West Research Ethics Committee; reference number: 18/YH/0385 (Appendix G).

Eligible participants were identified by their current respiratory clinician during a routine outpatient appointment. Participants who were eligible and expressed a preliminary interest were provided with a study pack which included further information and questionnaires to complete. Participants were given a choice to complete the study pack in the hospital and return it to their clinician or to take it home and post it back using the enclosed pre-paid envelope. Participants were offered to be included in a prize draw to win one of two £50 high street vouchers as an incentive for their participation. Participants were recruited between 04/02/2019 and 21/02/2020.

Study pack design

The study pack can be seen in Appendix L. It included a participant information sheet, consent form, demographic questionnaire, six questionnaires assessing psychological factors and asthma outcomes and a debriefing sheet.

Measures

Generalised Anxiety (GA)

Generalised Anxiety Disorder Questionnaire (GAD-7) [37] is a widely used and validated measure assessing the severity of anxiety symptoms. The total score ranges from 0 to 21, with a score ≥ 10 used as a cut-off indicating the presence of anxiety disorder [37-38]. Scores ≥ 5, ≥ 10 and ≥ 15 indicate mild, moderate and severe anxiety levels respectively. GAD-7 showed to have an excellent internal consistency (α = .92) and good test-retest reliability (ICC = .83) [37]. This was replicated in the current sample with GAD-7 showing excellent internal consistency with Cronbach's alpha. α =94.

Experiential avoidance (EA)

Brief Experiential Avoidance Questionnaire (BEAQ) [10] is a 15-item validated measure assessing EA – defined as an emotion regulatory style characterised by a tendency to control or avoid unpleasant internal experiences (including feelings, thoughts and physical sensations) [39]. A total score ranges from 15 - 90. A higher score is indicative of greater EA. BEAQ exhibited good internal consistency with Cronbach alphas ranging from .80 to .86 across clinical, community and student samples [10]. BEAQ also showed good test-retest reliability (r =.85) in a sample of chronic illness population [40]. The current sample showed good BEAQ's internal consistency (α=.90).

Self-efficacy (SE)

The Perceived Control of Asthma Questionnaire (PCAQ) [41] is an 11-item validated measure assessing individuals' perceived ability to manage their asthma. A total score ranges from 11-55, with a higher score indicating a greater perceived ability to control their asthma. In previous research using a sample of adults with asthma, the PCAQ showed good internal consistency (α = .79) and good construct validity [41]. The PCAQ also showed good internal consistency in the current sample (α = .83).

Asthma-Specific Quality of life (QoL)

Mini Asthma Quality of Life Questionnaire (MiniAQLQ) [42] is a validated 15-items tool measuring the impact of asthma on QoL in the past 2 weeks across the following four domains: asthma symptomatology, limitation of activities, emotions and environment. Total score ranges between 15 - 105. A higher score indicates a greater asthma-related QoL. In the development and validation study by Juniper et al. [42], MiniAQLQ showed good internal consistency with Cronbach alphas ranging from .80 to .89 for the total and individual domain scores, and a good ability to detect change over time. In the current sample, the internal consistency for the MiniAQLQ total score was α = .95.

Asthma Control

Asthma Control Test (ACT) [43] is a 5-item self-administered and validated questionnaire looking at individuals' level of asthma control over the past 4 weeks. Total ACT score ranges from 5-25. In the analysis, the total score was used as a continuous variable where a higher score indicated a better asthma control. Scores ≥20, 16-19 and < 16 indicate well-controlled, not well controlled and very poorly controlled asthma, respectively and were used in the current study to describe the sample. The ACT showed high internal consistency with Cronbach alphas ranging from .79 to .85 across studies using samples of adults with asthma attending asthma specialist clinic and subjects with both controlled and uncontrolled asthma [43,44]. ACT was also found to have good test-retest reliability (.77) [45]. ACT showed high correlation with other validated asthma control measure – Asthma Control Questionnaire (r = .89) [43]. The Cronbach's alpha for the current sample was .90.

Demographic variables

Data were also collected on various sociodemographic and asthma-related characteristics including participants' self-reported age, gender, smoking status, BMI (calculated using reported height and weight), number of cigarettes smoked per day, number of years living with asthma, number of courses of steroid medication in the past year, short-acting reliever inhaler usage in the last week (defined as the number of inhalations in the last week), number of Accident and Emergencies (A&E) visits and hospitalizations in the past year. Smoking status was categorized to "never smoked", "an ex-smoker", "currently a smoker". Courses of steroid medication were measured using the following 3 pre-specified categories "0", 1-3" and "4 or more".

Depression is a common co-morbidity in individuals with GA and was previously shown to be related to asthma morbidity. The Patient Health Questionnaire (PHQ-9) [46] is a validated tool assessing the severity of depressive symptoms. Total score ranges from 0-27. PHQ-9 demonstrated excellent internal consistency ($\alpha = .90$) [46]. The Cronbach's alpha for the current sample was .91.

Sociodemographic and asthma characteristics and levels of depression were assessed and included in the analyses as potential confounding variables.

Data Analysis Plan

All analyses were completed using the Statistical Package for Social Sciences (SPSS) version 24. SPSS EXPLORE, FREQUENCIES and DESCRIPTIVES functions were employed to explore the sample characteristics and to report relevant descriptive statistics. Analyses using SPSS EXPLORE and REGRESSION function were used to evaluate relevant assumptions regarding normality. Pearson's correlation coefficients were calculated to explore relationships between variables to a) evaluate assumptions regarding multicollinearity, b) identify any covariates significantly associated with outcome variables and c) explore associations between predictor, mediators, and outcome variables.

Mediation analyses were conducted using the PROCESS Model 4 procedure for SPSS version 3.4.1 [47]. As recommended by Preacher & Hayes [48] a bootstrapped sampling distribution (based on 10,000 bootstrapped samples) was used to estimate the unstandardized indirect effects, the standard error and 95 bias-corrected confidence

intervals (CI) for the ‘ab’ mediation path. Since the bootstrapping method does respect the non-normal distribution of the indirect effect, it has been recommended to be used with smaller samples with more confidence [48]. The inference regarding whether the ‘ab’ indirect effects are statistically significant will be evidenced by 95% bias-corrected bootstrap CI entirely above/below zero.

In separate mediation analyses, asthma morbidity indicators (asthma control, asthma specific QoL, SAARM use) were entered as outcome variables (y) and SE and EA as mediators (M). Generalize anxiety was entered as a predictor variable (x). The SAARM and steroid medication use and years living with asthma were entered as covariates in mediation models including asthma specific QoL and asthma control to account for their effects on the dependent variables.

3. Results

3.1. Recruited Sample

Response rate post hoc power analysis

A total of 203 eligible participants were identified by clinicians and were given a study pack to complete. Of those 65 participants have returned completed questionnaires, yielding a 32% return rate. This is in line with similar postal questionnaire studies conducted in adults with asthma [49]. Received questionnaires were screened and all responses were eligible for the inclusion in the study.

Post hoc analysis was conducted to explore power for the recruited sample (n=65). Given that mediation is based on regression analyses, we have calculated obtained power using the G power software. We have calculated that for four included regression models with 5 predictors (1 predictor, 1 mediator and 3 covariates), assuming medium effect the current sample reached the power of .62. The two regression models with 2 predictors (1 predictor and 1 mediator) reached the power of .78. However, since the current study used a bootstrapping method which does respect the non-normal distribution of the indirect effect, this is likely to be an underestimate of achieved power [48].

Missing data

The sample (n = 65) had a low rate of missing data (.28%) with < 5% of data missing for any individual case. Two individual items were missing for outcome variables, with the remaining items (n = 12) missing for demographic variables. The Little's Missing Completely at Random test showed that data for each variable were missing completely at random (MCAR), except for weight which was missing at random (MAR). Given that the current sample had < 25% of item scores missing in <10% of data, a single imputation (SI) method, namely Bayesian Stochastic Regression Imputation (BSRI) to item scores was used to deal with missing data [50]. This method was chosen over Complete Case analysis to preserve the variability of data and statistical power. The BSRI method to item scores was chosen over the multiple imputation as it previously showed to be more practical and produce equally accurate regression model in samples

with a small proportion of both MCAR and MAR data [50-52]. Compared to other SI methods, the BSRI showed to better account for the regression uncertainty not only by adding an error variance to the predicted values but also by accounting for the uncertainty in the regression coefficient estimation of the imputation model [53,54]. Differential analyses showed that there was not a significant ($p>.05$) difference between means for the imputed and the completed cases samples. Imputed data were therefore used to report sample characteristics and for all subsequent analyses.

Sample characteristics

The sample was explored with regards to their demographic, asthma specific and mental health characteristics and these are summarised in tables 2.1.,2.2., and 2.3. respectively.

As shown in Table 2.1., more than half of the recruited sample (56%) consisted of female participants. The mean age of the sample population was 52 years. For a high proportion of recruited individuals (77%) their Body Mass Index (BMI) score fell within the pre-obesity category and higher. Only a small proportion of the sample reported being current smokers (7.7%).

Table 2.1. Sample Characteristics - General

	Category	N	(%)
Gender	Male	28	(43.1)
	Female	37	(56.9)
Age group	16-19	2	(3.1)
[52.4 ± 15.6, 17-74]*	20-29	8	(12.3)
	30-39	2	(3.1)
	40-49	7	(10.8)
	50-59	25	(38.5)
	60-69	12	(18.5)
	70-75	9	(13.8)
BMI (kilogram/m2)**	Underweight (<18.5)	1	(1.5)
[30.4 ± 7.92, 16.3 - 68.7]	Normal weight (18.5-24.9)	14	(21.5)
	Pre-Obesity (25-29.9)	22	(33.8)
	Obesity Class 1 (30-34.9)	12	(18.5)
	Obesity Class 2 (35-39.9)	10	(15.4)
	Extreme Obesity Class 3 (>40)	6	(9.2)
Smoking status	Currently a smoker	5	(7.7)
	An ex-smoker	16	(24.6)
	Someone who has never smoked	44	(67.7)

*(Mean ± SD, range) ** **Classification [WHO, 2019]**

Asthma characteristics

Regarding asthma characteristics (summarized in Table 2.2.), individuals in the current sample reported living with asthma on average for 26 years. More than half of the recruited sample reported asthma symptoms which are very poorly controlled (57%). Majority of the sample was taking steroid medication (80%) with 43% reporting taking 4 or more courses of steroid medication in the past year. Individuals in the current sample reported relatively high reliance on their short-acting asthma reliever medication with reporting on average taking about 15 puffs in the past week.

Table 2.2. Sample Characteristics – Asthma Specific

	Category	N	(%)
Years living with asthma	0-4	7	(10.8)
[26.3 ± 16.6, 1-72]	5-9	6	(9.2)
	10-19	9	(13.8)
	20-29	15	(23.1)
	30-39	9	(13.8)
	40+	19	(29.2)
Asthma control (self-report)	Very poorly controlled (5-15)	37	(56.9)
(ACT total scores/past 4weeks)	Not well controlled (16-19)	8	(12.3)
[15.8 ± 5.9, 6-25]	Well Controlled (20-25)	20	(30.8)
Courses of Steroid medication	0	13	(20)
(12 months)	1-3	24	(36.9)
	4 or more	28	(43.1)
SAARM use (puffs/past week)	0	16	(24.6)
[15±2.3, 0-70]	1-9	14	(21.5)
	10-20	23	(35.4)
	20-29	3	(4.6)
	30-39	1	(1.5)
	40+	8	(12.3)
Health Care Utilisation	**E&R Visits:**		
(asthma-related) (12 months)	0	44	(67.7)
For those with E&R visit :	1-2	15	(23.1)
[Mdn = 2, 1-8, Q1=1; Q =2]~	3 or more	6	(9.2)
	Hospitalisations		
For those hospitalised:	0	43	(66.2)
[Mdn= 2, 1-7, Q1=1; Q3=3]~	1-2	17	(26.1)
	3 or more	5	(7.6)

*[Mean ± SD, range]; ~[Median, range, Quartile 1 and 3];

Majority of the sample (68% and 66% respectively) reported no E&R visits or hospitalisations in the past year due to their asthma. For those who visited E&R and were hospitalised, 2 instances were the most frequently reported value.

Mental health characteristics

Approximately three-quarters of the sample (75.4%) reported experiencing minimal to mild levels of anxiety, with one quarter (24.6%) reporting anxiety scores above the cut off for GA disorder. Similarly, majority of the sample (69.3%) reported minimal to mild symptoms of low mood, with a slightly higher proportion of the sample (30.8%) reporting symptoms of low mood above the cut off for depression.

Table 2.3. Sample Characteristics – Mental Health

	Category	N	(%)
Anxiety symptoms	Minimal anxiety severity (0-4)	37	(56.9%)
(past 2 weeks) (GAD-7)	Mild anxiety (5-9)	12	(18.5%)
[5.3 ± 6.0, 0-20]	Moderate anxiety (10-14)	8	(12.3%)
	Severe anxiety (15 or higher)	8	(12.3%)
Depression symptoms (past	Minimal depression severity (0-4)	33	(50.8%)
2 weeks) (PHQ-9)	Mild (5-9)	12	(18.5%)
[6.92 ± 6.7, 0-22]	Moderate (10-14)	7	(10.8%)
	Moderately severe (15 or higher)	13	(20.0%)

Table 2.4. illustrates scores for the independent, mediator and outcome variables. The sample mean scores for GA (GAD-7) and depression (PHQ-9) were 5.3 and 7, indicating mild levels of anxiety and low mood, respectively. The sample's mean score for EA (BEAQ) was 48.2 indicating a moderate level of EA. Individuals in the sample reported having a moderate perceived control over their asthma with PCAQ mean score of 36.8 and moderately high asthma-related QoL (MiniAQLQ) with a mean score of 69.2.

Table 2.4. Independent and Outcome Variables - Scores

Independent variables	Possible range	Lowest score	Highest score	Mean (SD)	↑
GAD-7	0-21	0	20	5.3 (6.0)	Higher symptom severity
PHQ-9	0-27	0	22	7.0 (6.7)	Higher symptom severity
BEAQ	15-90	15	84	48.2 (16.3)	Greater EA
PCAQ	11-55	15	54	36.8 (7.9)	Greater asthma SE
Outcome variables					
ACT	5-25	6	25	15.8 (5.9)	Greater asthma control
MiniAQLQ	15-105	24	105	69.2 (22.6)	Better QoL
SAARM use*	---	0	70	15.0 (2.3)	More weekly puffs

(GAD-7) - Generalized Anxiety Disorder – 7-items; (PHQ9) – Patient Health Questionnaire 9-items; (BEAQ) – Brief Experiential Avoidance Questionnaire; (PCAQ) – Perceived Control of Asthma Questionnaire; (ACT) – Asthma Control Questionnaire; (MiniAQLQ) – Mini Asthma Quality of Life Questionnaire; (SARI) – Short-Acting Asthma Reliever medication; EA = Experiential Avoidance; SE = Self-efficacy. *Puffs/week.

3.2. Analyses

Preliminary analyses

When dividing variables by their standard error for skewness and kurtosis all independent and outcome variables showed to be approximately normally distributed with skewness and kurtosis values within acceptable ranges (approximately +/- 1.96 for z score at p =.05) [55]. The Multicollinearity between predictor and demographic variables were assessed in SPSS by checking the variance inflation factors (VIF) and tolerance statistics. It was previously suggested that in smaller samples variables with VIF > 2.5 and tolerance < .2 are indicative of multicollinearity and should be assessed further [55]. All variables except for PHQ-9 and GAD-7 showed low VIF values (range between 1.1 and 1.6) and a tolerance >.2. suggesting no presence of multicollinearity. PHQ-9 and GAD-7 had higher VIF value of 3.1 and 2.6 respectively. These variables also showed to be highly intercorrelated ($r = .8$, $p < 0.001$) with a small Eigenvalue of .05 and .009, respectively. Removing highly correlated questionnaire item from PHQ-9 did not result in a reduction in multicollinearity. PHQ-9 was therefore removed from further analyses due to multicollinearity concerns. Removing PHQ-9 reduced VIF for GAD-7 to 1.8. Lastly exploring of scatterplots of residuals showed that all variables in the sample were approximately heteroscedastic.

Correlational analysis

The correlations between sample characteristics and study variables can be seen in table 2.5. The analysis identified significant associations between the hypothesised predictor - GA (GAD-7) and all hypothesised outcome variables: asthma control (ACT), asthma QoL (MiniAQLQ) and SAARM use. These were in expected direction. Greater anxiety was significantly correlated with poorer asthma control ($r= \mathbf{-.428}^{**}$, $p < .001$), poorer asthma related QoL ($r = \mathbf{-.540}^{**}$, $p < .001$) and higher use of SAARM ($r= \mathbf{.412}^{**}$, $p=.001$). Significant correlations were also found between GA and both hypothesised mediators: EA (BEAQ) ($r=\mathbf{.565}^{**}$, $p < .001$) and SE (PCAQ) ($r= \mathbf{-.525}^{**}$, $p < .001$).

Hypothesised mediators were then found to be significantly correlated with asthma control and asthma QoL in the expected direction. Greater EA (BEAQ) was associated with poorer asthma control (ACT) (r = **-.406**** , p = .001) and poorer asthma QoL (MiniAQLQ) (r = **-.519****, p<.001). Greater SE to control asthma (PCAQ) was linked to better asthma control (ACT) (r = **.498**** , p<.001) and QoL (MiniAQLQ) (**.634****, p<.001). Greater PCAQ was associated with higher SAARM use (**r = -.367**, p = .003). BEAQ was positively correlated with SAARM use in the expected direction but this association was just below a cut off for statistical significance (r = .024, p = .057). However, as per recent recommendations, the pattern of significance for individual 'a' and 'b' mediation paths does not necessarily indicate whether the indirect effect is significant [56]. The BEAQ will, therefore, be further explored as a mediator on the relationship between GA and SAARM to estimate the indirect effect. The SAAMR and steroid medication use and years living with asthma were significantly associated with both ACT and MiniAQLQ and were included as covariates in the relevant mediation analyses.

Table 2.5. Correlations between Sample Characteristics and Study Variables.

Variable	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17
(1) Age	1																
(2) Gender	-.088	1															
(3) BMI	-.053	-.049	1														
(4) Smoking status	.060	-.059	.203	1													
(5) Asthma duration	.256*	-.052	-.005	.095	1												
(6) A&E visit (Yes/No) ◆	.264*	-.316*	-.050	.189	.079	1											
(7) No of A&E visits ◆	-.332**	.083	-.076	-.135	-.081	-.713**	1										
(8) Hospital admission (Yes/No) ◆	.316*	-.031	-.166	.166	.083	.827**	-.625**	1									
(9) No of Hospital admissions ◆	-.443**	.183	.079	-.059	-.087	-.669**	.740**	-.773**	1								
(10) Steroid use (courses) ◆	-.021	.142	-.092	-.065	.170	-.310*	.234	.166	.236	1							
(11) PHQ9	-.349**	.018	.066	-.243	.167	-.473**	.520**	-.434**	.469**	.269*	1						
(12) GAD7	-.343**	.017	-.101	-.339**	.043	-.348**	.366**	-.320**	.347**	.172	.757**	1					
(13) BEAQ	-.065	-.092	-.251*	-.204	.132	-.309*	.224	-.174	.228	.094	.553**	**.565****	1				
(14) PCAQ	.313*	.027	-.051	.243	.021	.338**	-.304*	.287*	-.266*	-.198	-.562**	**-.525****	-.435**	1			
(15) ACT	.186	-.022	-.032	.059	**-.424****	.158	-.163	.144	-.142	**-.364****	**-.606****	**-.428****	**-.406****	**.498****	1		
(16) MiniAQLQ	.101	.049	-.012	.136	**-.405****	**.259***	-.222	.213	-.174	**-.375****	**-.702****	**-.540****	**-.519****	**.634****	.818**	1	
(17) SAARM use ◆◆	-.153	.013	.021	-.204	.189	-.211	**.360****	-.203	.166	.208	**.537****	**.412****	.238	**-.367****	-.690**	-.565*	1

(SARI) Short-acting asthma reliever medication use (puffs/past w) ◆ past 12 months ◆◆ past week $p \leq .05$, ** $p \leq .01$, a $N = 65$.

Mediation Analyses

Asthma control

The overall regression model predicting asthma control from GA and EA whilst controlling for the effects of steroid medication and SAARM use and years living with asthma was significant, explaining 62% of the variance in asthma control (r2 =.622, F (4, 60) = 24.71, p<.001). As displayed in Figure, the direct path from GA to asthma control was not significant. The mediation path (ab) from increased GA to decreased asthma control through increased EA was significant (b = -.110, SE = .049, 95% CI = [-.214, -.021]). According to Baron and Kenny [57], the presence of a significant indirect effect and non-significant direct effect is indicative of full mediation.

The second mediation analysis (displayed in Figure 2) explored a mediating effect of asthma control self-efficacy (SE) on the relationship between GA and asthma control whilst controlling for the effects of steroid medication, SAARM und years living with asthma. This regression model was significant explaining 62% of variance in asthma control (r2 =.622, F (24, 7) = 24.71, p<.001). There was a non-significant direct path from GA to asthma control. The 'ab' mediation path from increased GA to decreased asthma control through decreased asthma control SE was significant (b = -.117, SE = .061, 95% CI = [-.262, -.025]), indicating full mediation.

Figure 2.1. Mediation Pathway between Generalised Anxiety (GA) and Asthma Control through Experiential Avoidance (EA)

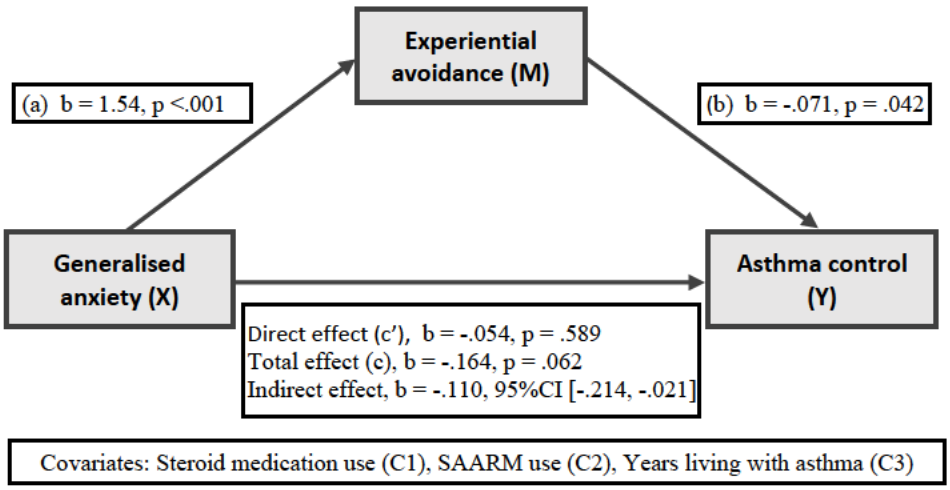
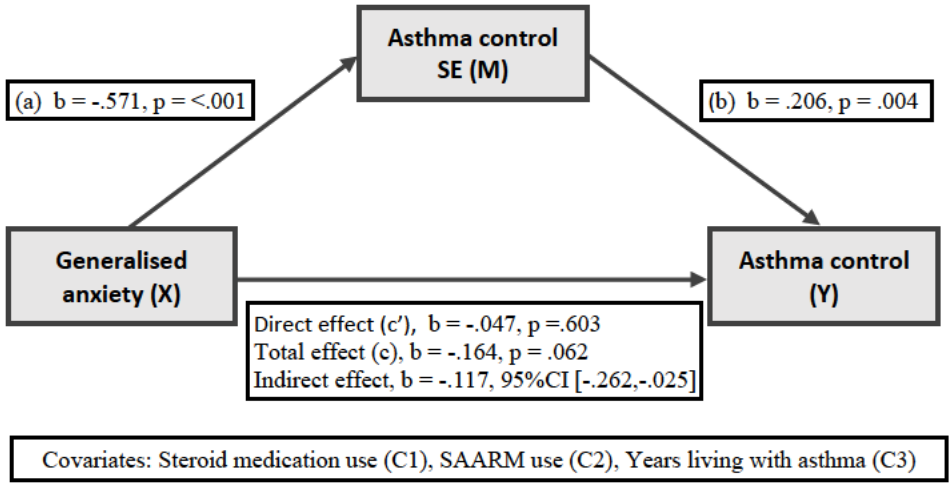


Figure 2.2. Mediation Pathway between GA and Asthma Control through Asthma Control Self-efficacy (SE)



Asthma Quality of Life (QoL)

Mediation pathway between GA and asthma QoL through EA, after accounting for covariates is displayed in Figure 3. The overall regression model was significant accounting for 57% of the variance in asthma QoL (r2 =.569, F (4, 60) = 19.81, p<.001). As displayed in Figure 3, the direct path from GA to asthma QoL was not significant. The mediation path (ab) from increased GA to decreased asthma control through increased EA was significant (b = -.582, SE = .259, 95% CI = [-1.16, -.137]), indicating full mediation.

To explore the effect of asthma control SE as a mediator in the relationship between GA and asthma QoL, whilst controlling for relevant covariates, a fourth mediation analysis was conducted (Figure 4). The overall regression model was significant, explaining 57% of variance in asthma QoL scores (r2 =.569, F (4, 60) = 19.81, p<.001). As displayed in Figure 4, the direct path from GA to asthma control was not significant. There was a significant effect for both 'a' and 'b' pathways as well as for the 'ab' indirect effect from increased GA to decreased asthma QoL through decreased asthma control SE (b = -.709, SE = .239, 95% CI = [-1.21, -.0253]), indicating full mediation.

Figure 2.3. Mediation Pathway between GA and asthma QoL through EA.

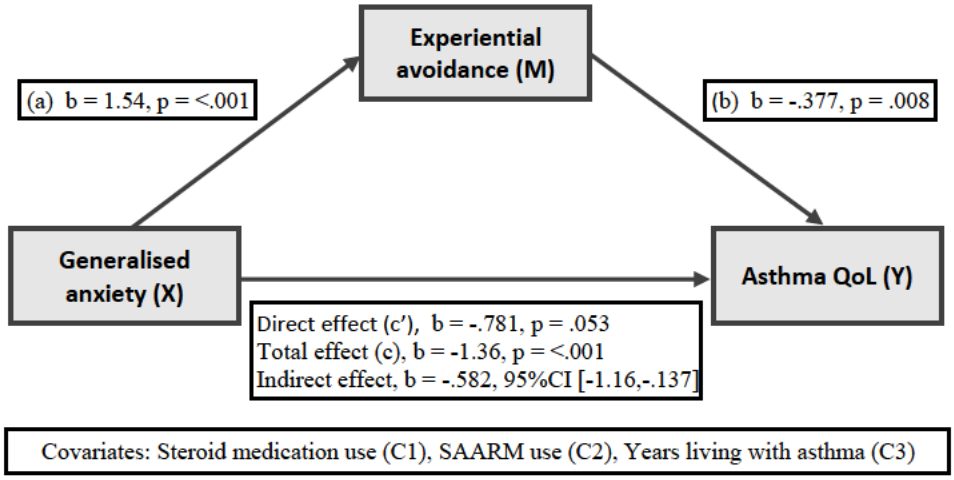
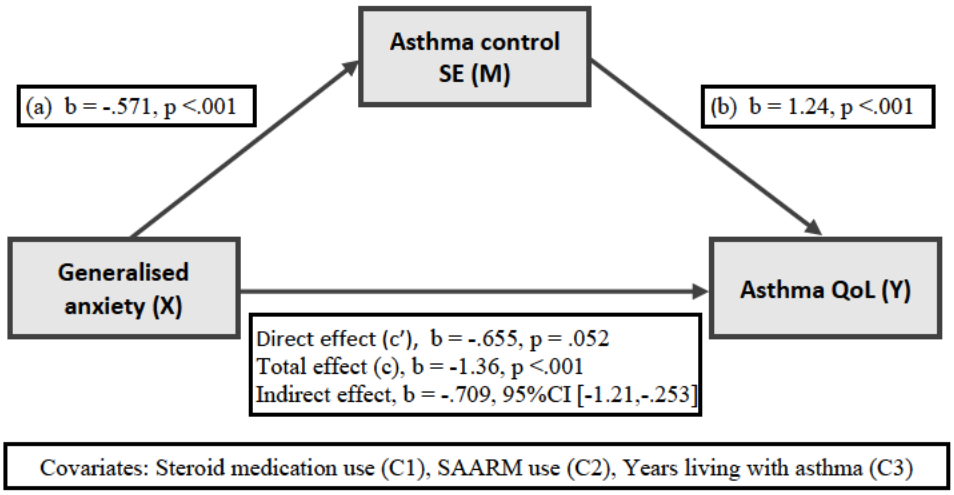


Figure 2.4. Mediation Pathway between GA and Asthma QoL through Asthma Control SE



Short-acting asthma reliever medication (SAARM) use

Two additional mediation analyses explored EA and asthma control SE as mediators in the relationship between GA and SAARM. The overall regression model for both mediators were significant, with both models accounting for an identical 17% of the variance in the SAARM use (R2 =.170, F(1, 63) = 12.91, p=.001). However, in both mediation analyses including EA and asthma control SE the direct path from GA to SAARM was significant (b = 1.26, p = .005 and b = .934, p = .026 respectively), whilst both indirect effects were n/s (b = .011, SE = .225, 95 % CI [-.445, .477] and b =.336, SE = .210, 95 % CI [-.027, .800] respectively), indicating absence of mediation.

4. Discussion

The first aim of the present study was to explore the relationship between GA, asthma control SE, EA, and asthma morbidity outcomes (asthma QoL, asthma control and SAAMR use) within a clinical sample of adults with asthma. In line with our hypotheses, the findings from the present study indicated that individuals with higher levels of GA presented with higher levels of EA, lower SE to manage their asthma and with poorer asthma morbidity outcomes. These included lower self-reported asthma control, asthma specific QoL and higher use of SAAMR use.

The link between higher levels of GA and lower asthma specific SE as well as asthma QoL and asthma control were in line with previous research in asthma population [6]. The found association between GA and EA was also consistent with results reported in the research literature from non-chronic health population [11-13], adding to the evidence base of EA in the asthma population. Our findings linking higher levels of EA with poorer asthma control and QoL were in line with research evidence from other chronic illnesses such as diabetes and HIV [14,15,16,17]. However, the majority of these studies used the AAQ questionnaire to measure EA which was previously widely criticised for its poor psychometric properties [27-29]. The current study was able to replicate these findings using BEAQ as a measure of EA. The BEAQ measure showed excellent reliability in the current sample. To our knowledge, this is a first study using BEAQ in a clinical sample of adults with asthma. It presents preliminary evidence of its usefulness as an alternative measure of EA.

In our study, higher EA was not linked to poorer medication compliance (as indicated by higher SAARM use), which was previously hypothesised based on findings from studies using samples with other chronic health conditions [14,15]. However, previous studies often focused on maintenance medication, and EA may have a different role when a relief medication is considered. It was initially hypothesised that individuals with higher EA are more likely to use higher doses of relief medication due to their lower tolerance of unpleasant asthma symptoms and tendency to cope with these by avoiding them. The fact that individuals with higher anxiety reported higher SAARM use, suggests that individuals might be misusing SAARM as a direct response to higher anxiety symptoms. Anxiety symptoms might be misperceived by individuals as asthma exacerbations. Higher SAARM might then be a direct attempt to manage a perceived health threat. It was previously suggested

that fear appraisals are faster and more automatic than appraisals related to unpleasant emotions which are likely to rely more on cognitive function and happen later in the process [58]. It is therefore likely that threat appraisals might happen independently and influence health behaviours differently. However, it is also possible that different variables not addressed in our study might play an indirect role. More research is needed to explore additional underlying mechanisms which might explain how GA influences higher SAAMR use.

As hypothesised, EA and SE mediated the relationship between GA and both asthma control and asthma QoL. This effect persisted after the potential confounding effect of steroid use, SAARM use and years living with asthma were controlled for.

One possible explanation for the mediation path from increased GA to decreased asthma control through increased EA is that individuals with higher GA tend to experience more unpleasant internal sensations (worries and associated unpleasant physical symptoms), have a greater tendency to evaluate these sensations as aversive and engage in avoidance to regulate these. Greater tendency to employ EA has previously been shown to further increase the frequency and intensity of suppressed internal experiences and intensify their emotional, cognitive, and physiological impact [e.g. 18-20]. This reciprocal relationship between anxiety and EA is likely to lead to a prolonged cycle of avoidance effort which depletes cognitive, attentional, and emotional resources needed to make appropriate behavioural choices and maintain goal-directed self-management behaviours [21]. Self-management behaviours, and required self-control, might in themselves trigger increased anxiety and be perceived as aversive. EA might result in adopting short term relieve alternatives or to avoid self-management behaviours altogether [22,23]. It is suggested that EA as a behavioural mechanism results in poorer self-management of asthma which is reflected in poorer control of asthma symptoms.

Since many of the same self-regulatory processes are needed to maintain valued activities, greater tendency to employ EA in individuals with higher anxiety is also likely to result in more restrictive lifestyle choices which impact on individual's asthma-related QoL. It is also important to note that due to the overlapping concepts in the ACT and MiniAQLQ measures, adequate control of symptoms is also likely to positively influence ones QoL scores, which rely on domains such as activities, social

roles and asthma-related restrictions which are all impacted on the experience of asthma symptoms and how well controlled they are.

A possible explanation for SE as a mechanism to explain how higher anxiety can lead to poorer asthma control might lie in the pervasiveness of GA symptoms which might often mimic and be misinterpreted as asthma symptoms as well as directly impact on asthma. In individuals with anxiety, this can lead to continuous negative feedback related to one's efforts to control their asthma. Such experience can undermine individuals perceived confidence in their ability to manage their asthma symptoms but also the usefulness of current self-management behaviours and health advice [59]. This can potentially decrease their motivation to engage in such behaviours (e.g. poorer compliance with medication regimens, etc., avoidance of asthma triggers, etc.), impacting on asthma control and QoL. Low SE has previously shown to be a well-established factor in the research literature associated with poor asthma control and asthma QoL [e.g. 6].

Despite findings in the general literature that individuals with higher levels of GA reported lower asthma control SE and higher EA [6, 11-13] and the evidence that lower asthma specific SE and EA correlates with poorer medication compliance including higher use of SAARM [6, 14,15] neither SE nor EA mediated the relationship between GA and SAARM. These results suggest that contrary to our hypothesis, in adults with asthma, GA only had a direct impact on SAARM, with increased levels of anxiety associated with higher SAARM use.

4.1. Limitations and future directions

Several limitations need to be considered when appraising the findings. First, due to the use of a cross-sectional design, no assertions can be made regarding causality in the observed relationships. Further research should employ prospective, longitudinal designs to examine whether improving SE skills and decreasing EA leads to improvements in asthma control and asthma QoL in adults with asthma and comorbid anxiety. These could also inform us whether having consistently low SE and high EA plays a specific role in the maintenance of poor asthma outcomes with regards to asthma control and asthma QoL. The study relied exclusively on a questionnaire design and self-report, which could have potentially introduced bias due to poor recall, concerns about confidentiality and social desirability and fatigue/poor concentration

completing measures. Where possible authors tried to reduce some of these biases by assuring participants about confidentiality and anonymity and by giving participants time to complete questionnaires in their own time. The effort to complete questionnaires could have also potentially discouraged participants with certain characteristics.

Finally, calculating adequate sample size to detect indirect effects is complex and more research is needed [35]. The current study calculated its sample size on the assumption that it would be adequate for multiple regression analyses, given that mediation is based on regression. What more, by using the Bayesian bootstrapping method which does not rely on the assumption of normality, findings from the employed sample, although relatively small, can be interpreted with more confidence. However, given the limited knowledge that currently exists regarding mediation power calculations, there remains a possibility that the current study was underpowered to detect significant indirect effects employing the current statistical technique used.

To limit participants burden, information about potentially important sample characteristics such as ethnicity were not collected. Individual's socio-cultural context has shown to be important in forming cognitions, beliefs and values regarding emotions and ways of expressing and coping with them [60]. Therefore, these are likely to moderate the relationship between GA, EA, and asthma outcomes. Future research should explore whether the relationship between anxiety, EA and asthma outcomes vary as a function of different socio-cultural context and beliefs. There also might be a weaker relationship between EA and asthma outcomes in individuals who have a wider range of "adaptive" strategies to regulate emotions. Future studies could employ more sophisticated models to investigate the effect of several emotion regulation strategies simultaneously.

Our study employed a clinical sample of NHS outpatients recruited from a secondary care respiratory and asthma specific clinics. These patients have typically more severe asthma and more complicated treatment regimens than samples drawn from the general population or primary care settings. This is likely to impact on their level of anxiety as well as influence their self-management behaviours and ways of coping with their emotions. Therefore, caution needs to be taken when applying our findings to samples from other settings. Further research employing samples of adults with asthma from additional clinical and non-clinical settings are needed to see if findings from the current study can be replicated in a wider asthma population.

However, given the link between the severity of asthma and anxiety, it is likely that our findings will be especially helpful for clinicians working with individuals with more severe or poorly controlled asthma.

Our sample also reported living with asthma for a long time (on average 26.3 years). Although the current study has controlled for the effect of this variable in the analyses, living with asthma longer can likely affect the relationship between anxiety, SE, EA, and asthma outcomes. Future research could explore the role of anxiety, SE, and EA in individuals at different stages of their asthma journey, e.g. I newly diagnosed adults.

Although steroid and SAARM use were controlled for in the analysis as indicators of asthma severity, these relied on self-report. Future studies could control for objective indicators of asthma severity such as lung function or use electronic momentary assessment devices to report SAARM use.

Despite the preliminary support for the importance of SE and EA as underlying mechanisms to explain the link between GA and asthma QoL and asthma control, it is important to note that these reflect only a small subset of potential psychological mechanisms. In recent research with adults with other chronic illnesses, it was suggested that factors such as self-regulation and illness representation present additional psychological factors which might account for variance in illness-specific outcomes in adults [61]. Future research is needed to explore these further in adults with asthma with co-morbid anxiety. Future studies which compare the role of GA compared to health anxiety would be of interest to see if they influence asthma outcomes differently or through different mechanisms.

4.2. Clinical implications

Notwithstanding these limitations, few studies have examined the relation of anxiety disorders to later physical health symptoms, or the processes that may explain this relation. The current study is the first to explore SE and EA as potential mechanisms linking anxiety and asthma outcomes within a clinical sample of adults with asthma in NHS Scotland settings. These findings add to existing research on the link between psychological factors and asthma morbidity by showing that EA and SE constitute a vulnerability factor for poorer asthma outcomes in adults with anxiety. These results hold significant implications for our understanding regarding specific intervention

components which might be beneficial to promote better asthma outcomes in this population.

Considering these results, when higher levels of GA are identified in individuals with asthma, including a routine measure of EA and SE in clinical practice, may be particularly beneficial to detect individuals at risk of developing poorer asthma outcomes. Brief, self-report measures such as those included in the current study are often free, quick to administer and complete. Similarly, a preventative approach which includes clinicians asking about patterns of EA and SE in individuals with higher anxiety levels can promote positive changes through discussion or through redirecting patients towards helpful practical support and resources. Since it has been suggested that coping with anxiety using EA can deplete individual's self-regulatory resources to self-management, where higher anxiety or EA is indicated clinicians should be mindful of simplifying self-management regimens where possible to reduce self-regulatory load. Supported self-management, written treatment plans and follow up telephone consultations could also lessen the impact of anxiety and EA on asthma symptoms

Our results are also in line with existing research on the treatment of GA, which emphasises the negative impact of avoidance as a strategy to cope with difficult internal experiences [11-13]. It is now well established that continuous use of avoidance often intensifies the experience of difficulties and play an important role in their maintenance [11-13]. Our results provide preliminary, empirical support for the utility of psychological interventions among adults with asthma with co-morbid anxiety which specifically focuses on EA as a treatment component to improve asthma outcomes. These include for example cognitive-behavioural therapy (CBT), Acceptance Commitment Therapy (ACT) and Mindfulness-based interventions.

For example, Cognitive behavioural therapy might help individuals to identify unhelpful beliefs associated with their tendency to avoid their internal experiences and to test these assumptions through behavioural experiments. This would help individuals to challenge their positive beliefs about the usefulness of avoidance and reduce their reliance on it to regulate emotions. Alternatively, components of ACT or Mindfulness-based interventions focusing on fostering non-judgmental awareness and acceptance of internal experiences might help individuals developing skills to stay present with them without negative judgement. This can facilitate the re-evaluation of previous assumptions and foster more functional coping to improve asthma outcomes.

ACT and mindfulness interventions have been found to mediated therapeutic outcomes for individuals with chronic conditions such as diabetes, epilepsy, chronic pain, cancer [25]. Some preliminary findings showed that psychological interventions targeting EA led to improved self-management behaviours in chronic health conditions such as diabetes [24,25]. CBT was found to improve asthma outcomes such as asthma control and asthma QoL in adults and adolescents with asthma [62]. However, further research is needed to evaluate these interventions in asthma patients, specifically targeting EA as a mechanism of change.

The role of self-management SE on illness outcomes in asthma and other chronic illness has been well established. This is reflected in current interventions which emphasise the importance of promoting illness-specific SE skills for managing illness [63]. The current study added to the SE evidence base by highlighting its role as a potential mechanism which links higher anxiety with poorer asthma outcomes. It suggests that interventions which might help individuals to distinguish between their triggers for asthma exacerbations and triggers for anxiety might help patients to feel more confident in their self-management skills and improve their SE. Regular feedback to patients regarding their asthma management, highlighting small successes and fostering a sense of ownership for their self-management might also promote higher confidence in managing asthma in adults with anxiety [63] Helping patients to learn how to self-monitor their asthma and encourage them to keep records of their management (e.g. self-monitoring diaries or goal-setting plans) might assist them in receiving regular feedback for their self-management [63,64]. Such feedback might be protective against the diminishing of their asthma control SE due to the negative cycle of asthma and anxiety.

Findings from our study suggest that interventions targeting anxiety (physical symptoms and anxious cognitions) directly might be beneficial to address high SAARM use.

5. Conclusions

The results from the present study suggest that individuals' asthma control SE and levels of EA mediate the relationship between GA and both asthma control and asthma QoL. These findings provide support for the utility of psychological interventions targeting SE and EA as important mechanisms of change to improve control of asthma symptoms and QoL in adults with asthma with co-morbid anxiety. These preliminary

findings also highlight that consideration of psychological co-morbidity in the asthma population is crucial as these have shown to be significantly associated with poorer asthma outcomes. The current study employed a clinical sample of adults with asthma receiving care from NHS outpatient respiratory services the results might be particularly relevant to clinicians working with individuals with more complex asthma difficulties in these settings.

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APPENDICES

APPENDIX AA: Description of Emotion regulation strategies (adapted from Aldao et al. 2010 and Marroquin et al. 2017)

Acceptance	• Recognising the existence of a problem/stressor and allowing oneself to experience a negative effect.
<u>Avoidance:</u> Cognitive avoidance Behavioural avoidance Denial	 • Strategy to mentally escape, minimise or distract oneself from situational demands. • Disengagement from the problem or stressor, giving up efforts to actively cope with the problem/situation. • Not acknowledging the existence or importance of the current problem, stressor or emotion experience.
Rumination Worry	• Passive, repetitive, abstract thinking style focusing on the causes and consequences of one's negative internal experiences. • Passive, recurrent and pervasive thinking style focusing on possible future scenarios/ negative outcomes of events/problems and attempts to solve these.
Emotion expression Emotion suppression	• Efforts to restrain or control verbal and non-verbal expressions of emotion experience. • Efforts to verbally or non-verbally communicate emotional experiences.
<u>Reappraisal:</u> Positive appraisal Cognitive reappraisal	 • A cognitive strategy which reconstructs the meaning of a situational demand or a problem as having a positive quality. • Mentally changing the initial response to a stressor (e.g. viewing the situation in a broader context).

APPENDIX A: EMBASE, PsychINFO, PsychARTICLES and MEDLINE search strategy (through the OVID electronic search interface).

Search Number	
Health condition of interest	
#1	"Asthma" OR “asthma*”
Emotion regulation strategy	
#2	"emot* regulat*" OR "emot* dysregulat*" OR “avoid*” OR “ruminat*” OF “reapprais*” OR “accept*” OR “suppress*” OR "problem solv*" OR "problem-solv*"
Asthma control outcomes	
#3	“asthma quality of life” OR “asthma-related quality of life” OR “asthma-specific quality of life” OR “AQL*” OR “AQoL*” OR “quality of life” OR “LWAQ” OR “Living with Asthma Questionnaire” OR “St. George's Respiratory Questionnaire” OR “SGRQ” OR “asthma control’ OR "self-manag*" or “self manag*” OR “adheren*” OR “nonadheren*” OR “non-adheren*” OR “complian*” OR “noncomplian*” OR “non-complian*”
Exclusion terms	
#4	"Animals" OR "not Humans"
#5	(#1 AND #2 AND # 3) NOT (#4)
Total with limits	
#6	[limit #6 to (English or Czech language and articles published between 1985 – 2019)]

“asthma quality of life” OR “asthma-related quality of life” OR “asthma-specific quality of life” OR “QoL*” OR “HQoL*” OR “H QoL*” OR “HRQoL*” OR “AQL*” OR “AQoL*” OR “LWAQ” OR “SGRQ” OR “asthma control” OR "self-manag*" or “self manag*”OR “adheren*” OR “nonadheren*” OR “non-adheren*” OR “complian*” OR “noncomplian*” OR “non-complian*”

APPENDIX B: Data extraction form

Publication details (author, year, and country)
Study design
Sample characteristics (population, age, gender, sample size)
Type of emotion regulation strategy and measure used
Primary and Secondary Outcomes and measures used
Statistical analysis
Correlation coefficient (r) or equivalent between relevant variables
Key findings regarding the relationship between emotion regulation strategy and primary/secondary outcomes

APPENDIX C: Downs and Black (1998) Quality Appraisal Checklist

REPORTING		
1	Is the hypothesis/aim/objective of the study clearly described?	Yes/No
2	Are the main outcomes to be measured clearly described in the Introduction or Methods section?	Yes/No
3	Are the characteristics of the patients included in the study clearly described?	Yes/No
4	Are the interventions of interest clearly described?	Yes/No
5	Are the distributions of principal confounders in each group of subjects to be compared clearly described?	Yes/Partially/No
6	Are the main findings of the study clearly described?	Yes/No
7	Does the study provide estimates of the random variability in the data for the main outcomes?	Yes/No
8	Have all important adverse events that may be a consequence of the intervention been reported?	Yes/No
9	Have the characteristics of patients lost to follow-up been described?	Yes/No
10	Have actual probability values been reported (*e.g.* 0.035 rather than < 0.05) for the main outcomes except where the probability value is less than 0.001?	Yes/No
EXTERNAL VALIDITY		
11	Were the subjects asked to participate in the study representative of the entire population from which they were recruited?	Yes/No/Unable to determine
12	Were those subjects who were prepared to participate representative of the entire population from which they were recruited?	Yes/No/Unable to determine
13	Were the staff, places, and facilities where the patients were treated, representative of the treatment the majority of patients receive?	Yes/No/Unable to determine
INTERNAL VALIDITY – BIAS		
14	Was an attempt made to blind study subjects to the intervention they have received?	Yes/No/Unable to determine
15	Was an attempt made to blind those measuring the main outcomes of the intervention?	Yes/No/Unable to determine
16	If any of the results of the study were based on 'data dredging', was this made clear?	Yes/No/Unable to determine
17	In trials and cohort studies, do the analyses adjust for different lengths of follow-up of patients, or in case-control studies, is the time period between the intervention and outcome the same for cases and controls?	Yes/No/Unable to determine
18	Were the statistical tests used to assess the main outcomes appropriate?	Yes/No/Unable to determine
19	Was compliance with the intervention(s) reliable?	Yes/No/Unable to determine
20	Were the main outcome measures used accurate (valid and reliable)?	Yes/No/Unable to determine
INTERNAL VALIDITY – CONFOUNDING		
21	Were the patients in different intervention groups (trials and cohort studies) or were the cases and controls (case-control studies) recruited from the same population?	Yes/No/Unable to determine
22	Were study subjects in different intervention groups (trials and cohort studies) or were the cases and controls (case-control studies) recruited over the same period of time?	Yes/No/Unable to determine
23	Were study subjects randomised to intervention groups?	Yes/No/Unable to determine
24	Was the randomised intervention assignment concealed from both patients and health care staff until recruitment was complete and irrevocable?	Yes/No/Unable to determine
25	Was there adequate adjustment for confounding in the analyses from which the main findings were drawn?	Yes/No/Unable to determine
26	Were losses of patients to follow-up taken into account?	Yes/No/Unable to determine
POWER		
27	Did the study have sufficient power to detect a clinically important effect where the probability	

APPENDIX D: Modified Downs and Black (1998) Quality Appraisal Checklist and scoring guide

External validity	Scoring
1. Representativeness of sample - Was the sample recruited representative of the entire asthma population from which they were recruited? Question 12 from the full checklist (Y=1, N/U=0)	A point was awarded if the study identified the source population for patients and described how the patients were selected. Patients were determined to be representative if they comprised the entire source population, an unselected sample of consecutive patients, or a random sample (only feasible where a list of all members of the relevant population exists). Where a study did not report the proportion of the source population from which the patients are derived, the question was answered as unable to determine.
Internal validity/bias	
2. **Data dredging** - If any of the results of the study were based on "data dredging", was this made clear? Question 16 (Y=1, N/U=0)	A point was awarded if no retrospective unplanned (at the outset of the study) subgroup analyses were reported.
3. **Appropriate statistical tests** - Were the statistical tests used to assess the main outcomes appropriate? Question 18 (Y=1, N/U=0)	If the distribution of the data (normal or not) was not described, it was assumed that the estimates used were appropriate, and a point was awarded. No point was awarded for studies that reported qualitative or quantitative data without any form of statistical comparisons or if the statistical tests reported were not appropriate.
4. **Appropriate outcome measures** – Were the main outcome measures used accurate (valid and reliable)? Question 20 (Y=1, N/U=0)	A point was awarded if the primary outcome measures were thought to be valid and reliable (e.g., the number of physical therapy visits per chart report), regardless of whether reliability or validity was reported. A point was not awarded if at least one of the primary outcome measures in the study was not valid or reliable or if this information was not reported or could not be determined (i.e., a questionnaire without reported validity or reliability).
Internal validity - confounding	
5. **Adjustment for confounding variables -** Was there adequate adjustment for confounding in the analyses from which the main findings were drawn? – Question 25 (Y=1, N/U=0)	A point was awarded unless the effect of the main confounders was not investigated or confounding was demonstrated, but no adjustment was made in the final analyses
Power	
6. **Size and power** - Did the study have sufficient power to detect a clinically important effect where the probability value for a difference being due to chance is less than 5%? Question 27 (Y=1, N/U=0)	A point was awarded if sample sizes were calculated * modified - A point was awarded if sample sizes were calculated and reported by authors and were deemed as having a sufficient power. If not reported power was calculated using G-power and point was awarded if power was larger than .70 with alpha set at 0.05, medium effect.

APPENDIX E: Methodological quality assessment of studies

Quality Criteria:	Study number:																	
	1	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**	**13**	**14**	**15**	**16**	**17**	**18**
External validity 1. Representative population: recruitment	+	+	-	+	+	-		-	-	-	+	+	-	-	-	+	-	+
Internal validity/bias 2. Data dredging	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
3. Appropriate statistical test	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+
4. Appropriate outcome measure(s)	-	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+
Internal validity: confounding 5. Adequate adjustment	+	+	+	+	+	-	-	-	-	+	+	-	+	+	-	-	-	+
Power* 6. Sample size (power)	+	+	-	+	-	+	+	-	-	+	+	+	-	-	-	+	+	+
Total/6	5	6	4	6	4	4	4	2	3	5	6	5	4	4	4	5	4	6
Methodological quality: Good (5-6) (A) Satisfactory (4) (B) Poor (<4) (C)	A	A	B	A	B	B	B	C	C	A	A	B	B	B	B	A	B	A

Criteria fulfilled: Yes = 1 (+) low risk of bias; No = 0 (-) high risk of bias; Unable to determine = 0 (?)
*modified– calculated as sufficient (G-power) (power > 0.70) or power calculated by authors as sufficient

APPENDIX F: PROSPERO Registration Form

The relationship between emotion regulation strategies and indicators of asthma control in adults with asthma: a systematic review
Lucie Michalova, Paul Graham Morris

Citation

Lucie Michalova, Paul Graham Morris. The relationship between emotion regulation strategies and indicators of asthma control in adults with asthma: a systematic review. PROSPERO 2019 CRD42019149928 Available from: https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42019149928

Review question

Does poorer emotion regulation predict worse asthma control outcomes in adults with asthma?

Searches

The following databases will be searched: EMBASE, PsycINFO and MEDLINE (via OVID interface). The search strategy will use a combination of each emotion regulation strategy and type of asthma control outcome in adult asthma population. These will include the following broad terms and associated MeSH subject headings: "accept*", "avoid*", "reapprais*", "suppress*" "problem-solv*", "ruminat*", "emotion* regulat*", "emot* dysregulat*, "self-manag*","asthma quality of life" and "asthma*". The search will be restricted to articles published between 1985 and 2019, available in English or Czech. The search will be limited to humans. The reference list of identified articles will be hand searched for additional relevant studies.

Types of study to be included

Studies will be included if they provided data regarding the relationship between the following emotion regulation strategies: acceptance, avoidance, problem-solving, reappraisal, rumination and suppression and primary asthma control outcomes in adults with asthma. Experimental or intervention studies will be included if they reported a baseline correlation between a specific emotion regulation strategy and primary outcomes. Non-correlational studies or studies which did not report the correlation, regression or similar data (and authors could not be contacted/provide this information) will be excluded. Single-case studies and qualitative-design studies will be excluded. Dissertations, theses, poster presentation and conference abstracts will be included if a sufficient study information can be obtained through manual search or contacting authors.
Studies which were not available in English or Czech will be excluded due to limited access to translation resources. Studies which measured a general emotion regulation score, without details regarding specific subscales will be excluded.

Condition or domain being studied

In this review emotion regulation has been conceptualized as conscious and unconscious processes through which individuals notice, make sense of and alter their emotional experiences (Bargh and Williams, 2007; Gross and Jazaieri, 201; Mauss, Bunge, and Gross, 2007). Using a classification of emotion regulation strategies used Aldao et al. (2010) meta-analysis, the current review will study: acceptance, avoidance, problem-solving, reappraisal, rumination and suppression.

Clinician-diagnosed asthma. If there are not enough studies identified in the asthma population, the search will be widened to include other chronic respiratory conditions (e.g. COPD) which are also associated with higher rates of treatment non-adherence and poorer self-management will be included.

Participants/population

Inclusion criteria: Studies will be included if they involve adults (from any nationality) over the age of 16 years with a diagnosis of asthma. Studies addressing both adults and children will be considered if the data provided for adults are reported separately or if the mean age is 16 years and over. Exclusion criteria: Studies will be excluded from the systematic review if they involve adults who experience comorbid health conditions which may have influenced their memory such as dementia, Parkinson's disease. Studies which used adults with comorbid substance misuse difficulties will also be excluded as substances can act as a form of emotion regulation (e.g. experiential avoidance).

Intervention(s), exposure(s)

Studies will be included in the current review if they employed a validated measure of an emotion regulation strategy, in line with specific subscales detailed in a recent meta-analysis by Aldao et al. (2010). Studies including a measure of acceptance and avoidance will be included if these were defined to assess acceptance/avoidance of thoughts, emotions and physical sensations. These will include studies looking at experiential avoidance (defined as an avoidance of thoughts, emotions and physical sensations), emotion avoidance or avoidance based emotional coping and avoidance of cognitive processes (e.g. distancing, distraction, etc.). To be included in the current review, studies will also have to include at least one of the primary outcomes at baseline.

Comparator(s)/control: Not applicable.

Context
Main outcome(s)
- Physiological and self-reported indicators of asthma control (e.g. lung function, asthma control self-reported
measures)
- Asthma medication adherence
- Asthma-related quality of life

Timing and effect measures

At baseline.

Additional outcome(s)

- Hospitalization for asthma
- Emergency room (A&E) utilization for asthma

Timing and effect measures

At baseline.

Data extraction (selection and coding)

The author (LM) will independently examine the search output and screen it by title and abstract. Using the outlined inclusion criteria, the full texts of potentially eligible studies will be retrieved and assessed for eligibility. The author will then extract data using an extraction form designed specifically for the review. Data on patient characteristics, emotion regulation strategy characteristics, study methods and outcome data will be retrieved.

Risk of bias (quality) assessment

The author (LM) will assess and appraise the quality of the included studies using the Downs and Black checklist (Downs & Black, 1998). This checklist will be adapted to appraise four areas of methodological quality: external validity, internal validity: bias, internal validity: confounding (selection bias) and power. Within these areas, six criteria will be considered for each selected study: (i) the representativeness of the study sample; (ii) the use and reporting of "data dredging" (iii) the appropriate use of statistical tests to assess outcomes; (iv) the appropriate use of outcome measures; (v) the adequate adjustments for confounding in the analyses from which the main findings were drawn; (vi) the sufficient power of the sample to detect clinically significant effects where the reported difference had less than 5% probability to occur by chance. A third of included studies will be randomly selected to be rated by a second reviewer (GOH). A disagreement between reviewers will be discussed and resolved by consensus. Selected articles will be rated according to whether they appropriately addressed (2 points), partially addressed (1 point) or did not address/unable to determine (0 points) each of the six criteria. A total score for each study will be calculated.

Strategy for data synthesis

Since methodological and statistical heterogeneity will likely preclude meta-analysis, the current review will employ quantitative narrative (descriptive) synthesis. It will be conducted by the main research (LM) and it will employ a three-stage narrative synthesis framework based on guidance for conducting narrative synthesis for systematic reviews by Popay et al. (2006). The synthesis will be an iterative process with the following stages overlapping:

1. Developing a preliminary synthesis of findings of included studies. This will involve organising findings from included studies to provide an initial description of patterns across the studies, specifically focusing on the direction and strength of the relationship of different emotion regulation strategies to asthma control outcome variables.

2. The above guidance will be used to explore relationships within and between studies and consider factors which might explain any heterogeneity in their findings, specifically in the direction and/or strength of the relationship between specified emotion regulation strategies and asthma control outcomes, drawing on the risk of bias assessments. Sources of potential heterogeneity may arise from study designs, populations, outcomes, contexts or study settings.

3. Assessing the robustness of synthesis. This will involve the main researcher (LM) appraising (1) the quality, (2) the relevance of the focus and (3) the extent of contribution of evidence towards answering the research question concerning the strength and direction of the relationship between specified emotion regulation strategies and asthma control outcomes from studies without high risk of bias.

Analysis of subgroups or subsets: None.

Contact details for further information: Lucie Michalova; s1687740@sms.ed.ac.uk

Organisational affiliation of the review: University of Edinburgh; www.ed.ac.uk

Review team members and their organisational affiliations: Ms Lucie Michalova. The University of Edinburgh; Dr Paul Graham Morris. The University of Edinburgh

Type and method of review: Narrative synthesis, Systematic review

Anticipated or actual start date: 10 August 2019; Anticipated completion date: 01 March 2020

Funding sources/sponsors: The University of Edinburgh

Conflicts of interest: None; Language: Czech, English; Country: Scotland; Stage of review: Review Ongoing

Subject index terms status: Subject indexing assigned by CRD; Subject index terms: Adult; Anxiety; Asthma; Emotions; Humans

Date of registration in PROSPERO: 31 October 2019; Date of publication of this version: 31 October 2019

Details of any existing review of the same topic by the same authors: n/a; Versions: 31 October 2019

Stage of review at time of this submission

Stage	Started	Completed
Preliminary searches	Yes	No
Piloting of the study selection process	Yes	No
Formal screening of search results against eligibility criteria	No	No
Data extraction	No	No
Risk of bias (quality) assessment	No	No
Data analysis	No	No

APPENDIX G: Evidence of favourable ethical opinion form Research Ethics Committee (REC)

Yorkshire & The Humber - Leeds West Research Ethics Committee
NHSBT Newcastle Blood Donor Centre
Holland Drive Newcastle upon Tyne
NE2 4NQ

Telephone: 0207 104 8086

14 December 2018

Lucie Michalova
[redacted]

Dear Lucie Michalova

Study title:	**Generalised anxiety and asthma morbidity: the mediating role of self-efficacy and experiential avoidance**
REC reference:	**18/YH/0385**
Protocol number:	**CAHSS1807/04**
IRAS project ID:	**235661**

Thank you for your letter of 9th December, responding to the Proportionate Review Sub-Committee's request for changes to the documentation for the above study.

The revised documentation has been reviewed and approved by the sub-committee.

We plan to publish your research summary wording for the above study on the HRA website, together with your contact details. Publication will be no earlier than three months from the date of this favourable opinion letter. The expectation is that this information will be published for all studies that receive an ethical opinion but should you wish to provide a substitute contact point, wish to make a request to defer, or require further information, please contact please contact hra.studyregistration@nhs.net outlining the reasons for your request.

Under very limited circumstances (e.g. for student research which has received an unfavourable opinion), it may be possible to grant an exemption to the publication of the study.

Confirmation of ethical opinion

On behalf of the Committee, I am pleased to confirm a favourable ethical opinion for the above research on the basis described in the application form, protocol and supporting documentation as revised.

Conditions of the favourable opinion

The REC favourable opinion is subject to the following conditions being met prior to the start of the study.

Management permission must be obtained from each host organisation prior to the start of the study at the site concerned.

Management permission should be sought from all NHS organisations involved in the study in accordance with NHS research governance arrangements. Each NHS organisation must confirm through the signing of agreements and/or other documents that it has given permission for the research to proceed (except where explicitly specified otherwise).

Guidance on applying for HRA and HCRW Approval (England and Wales)/ NHS permission for research is available in the Integrated Research Application System, at www.hra.nhs.uk or at http://www.rdforum.nhs.uk.

Where a NHS organisation's role in the study is limited to identifying and referring potential participants to research sites ("participant identification centre"), guidance should be sought from the R&D office on the information it requires to give permission for this activity.

For non-NHS sites, site management permission should be obtained in accordance with the procedures of the relevant host organisation.

Sponsors are not required to notify the Committee of management permissions from host organisations.

Registration of Clinical Trials

All clinical trials (defined as the first four categories on the IRAS filter page) must be registered on a publically accessible database. This should be before the first participant is recruited but no later than 6 weeks after recruitment of the first participant.

There is no requirement to separately notify the REC but you should do so at the earliest opportunity e.g. when submitting an amendment. We will audit the registration details as part of the annual progress reporting process.

To ensure transparency in research, we strongly recommend that all research is registered but for non-clinical trials this is not currently mandatory.

If a sponsor wishes to request a deferral for study registration within the required timeframe, they should contact hra.studyregistration@nhs.net. The expectation is that all clinical trials will be registered, however, in exceptional circumstances non-registration may be permissible with prior agreement from the HRA. Guidance on where to register is provided on the HRA website.

It is the responsibility of the sponsor to ensure that all the conditions are complied with before the start of the study or its initiation at a particular site (as applicable).

Ethical review of research sites

The favourable opinion applies to all NHS sites taking part in the study, subject to management permission being obtained from the NHS/HSC R&D office prior to the start of the study (see "Conditions of the favourable opinion" above).

Approved documents

The documents reviewed and approved by the Committee are:

Document	*Version*	*Date*
Evidence of Sponsor insurance or indemnity (non NHS Sponsors only) [Clinical Trial Liability]	V1	11 September 2018
GP/consultant information sheets or letters [GP Letter V1 11 September 2018]	V1	11 September 2018
IRAS Application Form [IRAS_Form_03122018]		03 December 2018
Non-validated questionnaire [Demographic Information Sheet V1 11 September 2018]	V3	07 December 2018
Other [Certificate of Employers' Liability Insurance]	V1	11 September 2018
Other [PL Confirmation]	V1	11 September 2018
Other [Professional Indemnity Confirmation]	V1	11 September 2018
Other [Participant Debrief Form V1 11 September 2018]	V3	30 November 2018
Other [PPI feedback]		25 November 2018
Other [Participant Debrief Form V1 11 September 2018]	V4	07 December 2018
Other [Response to provisional opinion]	V1	09 December 2018
Participant consent form [Participant Consent Form V1 11 September 2018]	V4	07 December 2018
Participant information sheet (PIS) [Participant Information Sheet V1 11 September 2018]	V4	07 December 2018
Referee's report or other scientific critique report [Thesis_Proposal_R1_Supervisor feedback V1 17 September 2018]	V1	17 September 2018
Referee's report or other scientific critique report [Thesis_Proposal_R1_University peer scientific review comments V1 13 July 2017]	V1	13 July 2017
Research protocol or project proposal [Study protocol V1 11 September 2018]	V4	07 December 2018
Summary CV for Chief Investigator (CI) [CV_CI V1 11 September 2018]	V1	11 September 2018
Summary CV for student [CV_CI V1 11 September 2018]	V1	11 September 2018
Summary CV for supervisor (student research) [CV Academic supervisor V1 11 September 2018]	V1	11 September 2018
Validated questionnaire [Questionnaires V1 11 September 2018]	V4	07 December 2018

Statement of compliance

The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

After ethical review

Reporting requirements

The attached document "After ethical review – guidance for researchers" gives detailed guidance on reporting requirements for studies with a favourable opinion, including:

- Notifying substantial amendments
- Adding new sites and investigators
- Notification of serious breaches of the protocol
- Progress and safety reports
- Notifying the end of the study

The HRA website also provides guidance on these topics, which is updated in the light of changes in reporting requirements or procedures.

Feedback

You are invited to give your view of the service that you have received from the Research Ethics Service and the application procedure. If you wish to make your views known please use the feedback form available on the HRA website:
http://www.hra.nhs.uk/about-the-hra/governance/quality-assurance

We are pleased to welcome researchers and R & D staff at our RES Committee members' training days – see details at http://www.hra.nhs.uk/hra-training/

18/YH/0385	**Please quote this number on all correspondence**

With the Committee's best wishes for the success of this project.

Yours sincerely

pp

Dr Rhona Bratt Chair

Email: nrescommittee.yorkandhumber-leedswest@nhs.net
Enclosures: *"After ethical review – guidance for researchers"*

Copy to: *Ms Charlotte Smith*
Mrs Liz Coote, R & D Manager, NHS Tayside

APPENDIX H: NHS Fife R&D Approval

Medical Director

Hayfield House
Hayfield Road
KIRKCALDY
KY2 5AH

NHS Fife

Miss Lucie Michalova
NHS Tayside
Dundee Adult Psychological Therapies Service
15 Dudhope Terrace
Dundee
DD3 6HH

20 December 2018

Our Ref *18-064*
18/YH/0385
Enquiries to *Aileen Yell*
E-mail *aileenyell@nhs.net*
Telephone *01383 623623 Ext 20940*
Website *www.nhsfife.org*

Dear Miss Michalova

Project Title: The role of generalised anxiety in asthma morbidity

Thank you for your application to carry out the above project. Your project documentation (detailed below) has been reviewed for resource and financial implications for NHS Fife and I am happy to inform you that NHS permission for the above research has been granted on the basis described in the application form, protocol and supporting documentation. The documents reviewed were:

Document	Version	Date
IRAS R&D Form	5.9.1	11 September 2018
GP Letter	1	11 September 2018
Protocol	4	7 December 2018
Demographic Information Sheet	3	7 December 2018
Participant Debrief Form	4	7 December 2018
Participant Information Sheet	4	7 December 2018
Participant Consent Form	4	7 December 2018
Questionnaires	4	7 December 2018
REC final favourable opinion letter		14 December 2018

The terms of the approval state that you are the Principal Investigator authorised to undertake this study within NHS Fife.

I note that the favourable ethical opinion applies to all NHS sites taking part in the study therefore no separate Site Specific Review is required in this case. The sponsors for this study are University of Edinburgh. Please note that it is the responsibility of the Sponsor to ensure that adequate and appropriate insurance is maintained throughout the course of the study.

Details of our participation in studies will be included in annual returns we are expected to complete as part of our agreement with the Chief Scientist Office. Regular reports of the study require to be submitted. Your first report should be submitted to Dr A Wood, R&D Manager, R&D Department, Queen Margaret Hospital, Whitefield Rd, Dunfermline, KY12 OSU (Amanda.wood3@nhs.net) in 12 months time and subsequently at yearly intervals until the work is completed. A Lay Summary will also be required upon completion of the project.

In addition, approval is granted subject to the following conditions:-

NHS Fife was awarded the Carbon Trust Standard in February 2010 and is the first Scottish NHS Board to achieve this accolade.

NHS
Fife

All research activity must comply with the standards detailed in the UK Policy Framework for Health and Social Care Research http://www.nhsresearchscotland.org.uk/uploads/tinymce/uk-policy-framework-health-social-care-research.pdf, health & safety regulations, data protection principles, other appropriate statutory legislation and in accordance with Good Clinical Practice (GCP).

Any amendments which may subsequently be made to the study should also be notified to Aileen Yell, R&D Research Coordinator (aileenyell@nhs.net) , as well as the appropriate regulatory authorities. Notification should also be given of any new research team members post approval and/or any changes to the status of the project.

This organisation is required to monitor research to ensure compliance with the Research Governance Framework and other legal and regulatory requirements. This is achieved by random audit of research. You will be required to assist with and provide information in regard to monitoring and study outcomes (including providing recruitment figures to the R&D office as and when required).

As custodian of the information collated during this research project you are responsible for ensuring the security of all personal information collected in line with NHS Scotland IT Security Policies, until the destruction of this data.

Permission is only granted for the activities for which a favourable opinion has been given by the REC (and which have been authorised by the MHRA where appropriate).

The research sponsor or the Chief Investigator or local Principal Investigator at a research site may take appropriate urgent safety measures in order to protect research participants against any immediate hazard to their health or safety. The R&D office (aileenyell@nhs.net) should be notified that such measures have been taken. The notification should also include the reasons why the measures were taken and the plan for further action. The R&D office should be notified within the same time frame of notifying the REC and any other regulatory bodies.

I would like to wish you every success with your study and look forward to receiving a summary of the findings for dissemination once the project is complete.

Yours sincerely

DR FRANCES ELLIOT
Medical Director
NHS Fife

Cc : Aileen Yell, R&D Research Coordinator, NHS Fife, Queen Margaret Hospital, Dunfermline
Dr Devesh Dhasmana, Consultant, NHS Fife

APPENDIX I: The REC Approval of a Substantial Amendment

NRSPCC, Nhsg (NHS GRAMPIAN)

Fri 21/06/2019 15:17

To:cahss.res.ethics@ed.ac.uk <cahss.res.ethics@ed.ac.uk>; MICHALOVA, Lucie (NHS TAYSIDE) <l.michalova@nhs.net>;

Cc:R&D.GenericReviews@ggc.scot.nhs.uk <R&D.GenericReviews@ggc.scot.nhs.uk>; YELL, Aileen (NHS FIFE) <aileenyell@nhs.net>; WOOD, Amanda (NHS FIFE) <amanda.wood3@nhs.net>;

Hi Everyone

Please see the categorisation re-issue below to correct a typo in the implementation date (it previously indicated 09.17.19).

Apologies for my error
Pam

A

Amendment Categorisation and Implementation Information

Dear Lucie

IRAS Project ID:	**235661**
Short Study Title:	**The role of generalised anxiety in asthma morbidity**
Date complete amendment submission received:	**04.06.19**
Sponsor Amendment Reference Number:	**N/A**
Sponsor Amendment Date:	**29.04.19**
Amendment Type	**Non Substantial**
Implementation date in NHS/HSC organisations in Northern Ireland and/or Scotland	**09.07.19 (providing conditions are met)**
For NHS/HSC R&D Office information	
Amendment Category	**A**

Thank you for submitting an amendment to your project. We have now categorised your amendment and please find this, as well as other relevant information, in the table above.

What should I do next?

Please read the information in IRAS, which provides you with information on how and when you can implement your amendment at NHS/HSC sites in each nation, and what actions you should take now.

If you have participating NHS/HSC organisations in any other UK nations please note that we will forward the amendment submission to the relevant national coordinating function(s).
If not already provided, please email to us any regulatory approvals (where applicable) once available.

When can I implement this amendment?

You may implement this amendment in line with the information in IRAS.
Please note that you may only implement changes described in the amendment notice.

Information relating to the addition of new sites

Your amendment also adds new participating NHS/HSC organisations to the study. The 35 day implementation date does not apply to the new sites. Please set up new sites as detailed below (as processes change from time to time, we recommend that you refer to the most up to date guidance about site set up, found within IRAS).

If your study is supported by a research network, please contact the network as early as possible to help support set up of the new site(s).

For new sites in Northern Ireland and/or Scotland:	Please start to set up your new sites. Sites may not open until NHS/HSC management permission is in place.

Who should I contact if I have further questions about this amendment?
If you have any questions about this amendment please contact the relevant national coordinating centre for advice:

- England – hra.amendments@nhs.net
- Northern Ireland – research.gateway@hscni.net
- Scotland – nhsg.NRSPCC@nhs.net
- Wales – research-permissions@wales.nhs.uk

Additional information on the management of amendments can be found in the IRAS guidance.

User Feedback

We are continually striving to provide a high quality service to all applicants and sponsors. You are invited to give your view of the service you have received and the amendment procedure. If you wish to make your views known please use the feedback form available at: http://www.hra.nhs.uk/about-the-hra/governance/quality-assurance/.

Please do not hesitate to contact me if you require further information.

Kind regards
Pam

Pamela Shand
Senior Administrator
NRS Permissions CC Team
Tel: 01224 552690
Email: nhsg.NRSPCC@nhs.net

APPENDIX J: NHS Greater Glasgow and Clyde R and D Approval

Administrator: Mrs Elaine O'Neill
Telephone Number: 0141 314 4001
E-Mail:
Website: https://www.nhsggc.org.uk/about-us/professional-support-sites/research-development/

Clinical Research & Development
Dykebar Hospital, Ward 11
Grahamston Road
Paisley, PA2 7DE
Scotland, UK

09 September 2019

Dr Rekha Chaudhuri
Department of Respiratory Medicine
Gartnavel General Hospital
1053 Great Western Road
Glasgow G12 0YN

NHS GG&C Board Approval

Dear Dr R Chaudhuri,

Study Title:	Generalised anxiety and asthma morbidity: the mediating role of self-efficacy and experiential avoidance
Principal Investigator:	Dr Rekha Chaudhuri
GG&C HB site	Gartnavel General Hospital
Sponsor	University of Edinburgh
R&D reference:	GN19RM322
REC reference:	18/YH/0385
Protocol no: (including version and date)	V5; 29/04/18

I am pleased to confirm that Greater Glasgow & Clyde Health Board is now able to grant **Approval** for the above study.

Conditions of Approval

1. **For Clinical Trials** as defined by the Medicines for Human Use Clinical Trial Regulations, 2004

    a. During the life span of the study GGHB requires the following information relating to this site
        i. Notification of any potential serious breaches.
        ii. Notification of any regulatory inspections.

It is your responsibility to ensure that all staff involved in the study at this site have the appropriate GCP training according to the GGHB GCP policy (www.nhsggc.org.uk/content/default.asp?page=s1411), evidence of such training to be filed in the site file.

2. **For all studies** the following information is required during their lifespan.
    a. First study participant should be recruited within 30 days of approval date.
    b. Recruitment Numbers on a monthly basis

NHS
Greater Glasgow and Clyde

c. Any change to local research team staff should be notified to R&D team
d. Any amendments – Substantial or Non Substantial
e. Notification of Trial/study end including final recruitment figures
f. Final Report & Copies of Publications/Abstracts

Please add this approval to your study file as this letter may be subject to audit and monitoring.

Your personal information will be held on a secure national web-based NHS database.

I wish you every success with this research study

Yours sincerely,

Mrs Elaine O'Neill
Senior Research Administrator

Cc: Lucie Michalova (NHS Tayside)
Charlotte Smith (The University of Edinburgh)

APPENDIX K: Sponsor Classification Letter – A Non-substantial Amendment

Non-Substantial Amendment 06 September 2019

BALL Carol
Fri 06/09/2019 15:48
To: MICHALOVA Lucie <s1687740@sms.ed.ac.uk>

Sponsor Amendment Classification	
Title:	**The role of generalised anxiety in asthma morbidity**
REC Reference	**18/YH/0385**
Sponsor Reference:	**Non-Substantial Amendment 06 September 2019**
Chief Investigator:	**Ms Lucie Michalova**

Dear Lucie

I have reviewed your proposed changes as outlined in our previous correspondence. .
I can confirm that in the opinion of the Sponsor's representative the following changes:

- ***Extension of end date to 30th April 2020***

Comprise a **non-substantial amendment**.

What to do next...	
REC	There is no requirement to inform the REC of this amendment
NHS R&D	You are obliged to inform the relevant NHS R&D group of your proposed changes. You should provide the same details as you provided to me, plus any amended supporting documentation. For multi-site studies, please contact NRS: nhsg.NRSPCC@nhs.net. **Please copy me into this correspondence.**

** **Note that you cannot implement the amendment until such time as approval has been given by R&D.**
**

Please copy me into, or forward on all correspondence with R&D.

I hope that helps, please get in touch if anything is unclear.

Best wishes,

Carol

Research Governance Administrator
College of Arts, Humanities & Social Sciences

The University of Edinburgh
Room B.13, 57 George Square
Edinburgh, EH8 9JU

t: +44 (0)131 651 3916 e: ;
w: www.accord.scot w: www.ed.ac.uk/cahss

accord
Academic and Clinical Central Office for Research and Development

APPENDIX L: Study pack (including the Participant Information Sheet, Consent Form, Questionnaires and Debrief Form)

Study title: What psychological factors influence asthma outcomes?

The Role of Generalized Anxiety in Asthma Morbidity: Self-efficacy and Experiential Avoidance as Mediators

Research team:

Lucie Michalova, Trainee Clinical Psychologist (Chief Investigator); Dr Devesh Dhasmana, Respiratory Consultant, NHS Fife (Principal Investigator); Dr Paul Morris, Lecturer, the University of Edinburgh (Academic Supervisor); Prof Kevin Power, Head of NHS Tayside Psychological Therapies Service (Clinical Supervisor); Dr Rekha Chaudhuri, Associate Specialist and Hon Clinical Associate Professor, NHS Greater Glasgow and Clyde (Principal Investigator) and Dr Freda Yang, Research Fellow, NHS Greater Glasgow and Clyde (Associate Investigator)

PARTICIPANT INFORMATION SHEET

Study title: What psychological factors influence asthma outcomes?

My name is Lucie Michalova. I'm doing a research study as part of my training course to become a Clinical Psychologist and I'm inviting you to take part in my study. Before you decide whether to take part, it is important you understand why I'm doing the research and what it will involve.

Please take time to read the following information carefully to decide whether you want to take part. You might want to talk it over with others. If anything isn't clear, or if you want to find out more, feel free to get in touch – my contact details are at the end of this form. This information sheet is yours to keep.

What's the study for?

In recent years it's become clear that psychological factors influence how well people fare with their asthma. Many people with asthma have generalised anxiety (frequent and uncontrollable worries about nothing in particular) and this linked to poorer asthma control, poorer asthma-related quality of life and the need to use asthma reliever medication more often. But the reason for this link is unclear. I'm interested in finding out whether a person feeling lacking confidence in managing their asthma and their ability to cope with unpleasant physical and emotional symptoms can explain how anxiety can lead to poorer asthma outcomes.

I hope my study will give a better understanding of what psychological factors influence asthma outcomes and help to develop better asthma treatments.

Why have I been invited?

Because you are aged between 16 and 75 and go to the Outpatient Asthma Clinic. Everyone we ask to take part will also have a diagnosis of asthma, good spoken and written English and currently don't have other chest problems other than asthma (e.g., chronic bronchitis, cystic fibrosis, chronic obstructive pulmonary disease, HIV-related lymphocytic airway inflammation) which are more problematic. Through speaking to you and checking your medical file, the doctor/nurse who looks after your asthma identified you as a potential participant.

Before you decide whether you would like to take part

Please note that due to the nature of the study I can't invite people who are currently having an episode of a serious mental illness e.g. psychosis, have a diagnosis of

fibromyalgia and/or are currently abusing substances (e.g. alcohol, drugs). Please only continue with the rest of the study pack if these do not apply to you. You can still take part if your circumstances change before the data collection period has finished on 30/04/20. If you want to discuss why you can't take a part, please feel free to contact me (Lucie Michalova) on the number below.

What will I be asked to do if I decide to take part?

If you are interested in taking part in this study, you will need to go through this information sheet and carefully read the information included. You can get in touch with me using the contact details below if you want to ask any questions about the study.

If you do want to take part, we'll ask you to open your study pack and read through a consent form. This says that you understand what the study involves, and you agree to take part in the study. If you agree to take part, we'll ask you for some basic information about you and your asthma. After this, we'll ask you to complete 6 short questionnaires about your anxiety, mood, asthma related quality of life, the way you manage emotions, your perceived confidence in managing asthma and questions about your current asthma management. This should take on average about 20 minutes. You'll only need to fill these questionnaires in once.

You can complete the study pack in the hospital if you want and hand it to the reception staff - or take it home and send it back using the pre-paid envelope. This will make sure you have as much time as you feel you need to think about taking part in the study and ask any questions you might have. It will also allow you to fill in the questionnaires when it suits you.

Do I have to take part?

No, it is your choice. Taking part is entirely voluntary. If you do decide to take part, you are still free to change your mind up until the point of sending out/returning your study pack. After that you can't. This is because all the responses in the study packs are anonymous and once, we've got yours back, we can't link you to your responses. If you decide not to take part, that will not affect the standard of care you get.

What are the possible disadvantages and risks of taking part?

Risks are minimal. The questionnaires have been used by other clinical and research teams. There is no evidence that completing the questionnaires will harm you. However, you may find some of the thinking and concentration tasks frustrating if you are not sure of the answers. You may also find filling in the questionnaires tiring and some questions may make you think about difficult experiences which could upset you. If you find some questions upsetting, you do not have to answer them. If you

become upset or concerned about your asthma or mental health, you can speak to your GP or a member of your clinical team.

What are the possible advantages and benefits of taking part?

After you've completed the questionnaires, you'll be asked if you wish to be included in a prize draw to have a chance of winning one of two £50 gift cards of your choice (Amazon/Tesco/Boots/Sainsburys/ASDA/John Lewis). You may also feel that by taking part you'll contribute to a greater understanding of psychological factors that influence how well people with asthma fare.

Will my participation in this study be kept confidential?

Yes. We'll keep all the information confidential. We'll comply with the strict laws which safeguard your privacy at every stage of the study.

After you have completed the questionnaires, any identifiable information will be removed and replaced by a code. There will be a unique study number assigned to your questionnaires. Although some of the other researchers involved in the study might look at your data, they won't know it's yours.

If you tell us any information during the data collection stage of this study which indicated any risk of harm to you or other people around you, I will have to tell someone. This is to make sure that you and other people are safe. I will only speak to a qualified member of staff, usually your GP, but I would discuss this with you first.

What happens when the study is finished?

After completing the questionnaires, you'll have the chance to tell me how taking part in the study was for you. You can also discuss your experience with one of your carers at the clinic if you like.

After I have finished analysis, anonymised electronic data will be archived within the University of Edinburgh for 10 years from the end of the project, with a review then and every following 5 years to decide whether data should continue to be stored or whether it should be securely deleted. Anonymised questionnaires will be held securely in a locked filing cabinet within the NHS Tayside premise until the departmental guidelines deem it appropriate to destroy them.

What will happen to the results of the research study?

I'll write them up as part of my course work and submit them to the University of Edinburgh as part of my training for my Doctorate of Clinical Psychology. I also want to get the results of this study published in an academic journal and present the results to interested groups and conferences to help clinicians across the world have

a better idea of different psychological factors influencing asthma outcomes. The results will be anonymised. This means that you won't be named or identified.

Can I find out the results of the study?

Yes. You will be able to see the results from the study and any associated publications on the project website. Go to: https://www.wiki.ed.ac.uk/x/W_xlFQ. Hopefully this will be from May 2020.

How can I find out if I won a prize?

If you agreed to be included in a prize draw, you will be asked to keep your Prize draw number which you can find at the of the debriefing sheet. The Prize draw will take place on 29th May 2020. Winning numbers will be published on the project website: https://www.wiki.ed.ac.uk/x/W_xlFQ on the same day with details of how to get in touch to claim the prize. Winners will have until 30th June 2020 to get in touch. If you forgotten the link to the study website or don't have access to the internet, please contact me on the number above.

Who has reviewed the study?

All research in the NHS is looked at by an independent group of people called a Research Ethics Committee. Yorkshire and the Humber – Leeds West Research Ethics Committee thinks my study is ethical. NHS management has also approved it.

Contacts:

If you have any further questions about the study, get in touch with me, Lucie Michalova via Linda Scott on: 01382 346160 or email:

If you would like to discuss this study with someone independent of the study team, please contact: Geraldine O'Hagan via Linda Scott on: 01382 346160 or email:

If you wish to make a complaint about the study, please contact NHS Fife: Patient Relations Department, Room 104, Hayfield House, Hayfield Road, Kirkcaldy, KY2 5AH, Tel: 01592 648153, Email: patientrelations.fife@nhs.net

or

NHS Greater Glasgow and Clyde: Complaints Department, North East Sector Offices, Stobhill Hospital, 300 Balgrayhill Road, Glasgow, G21 3UR, Tel: 01412 014500, Email: complaints@ggc.scot.nhs.uk.

Consent Form

Title:	**What psychological factors influence asthma outcomes?**
Protocol Number:	Version 6, 4 November 2019
Project Sponsor:	Edinburgh University
Chief Investigator:	Lucie Michalova, Trainee Clinical Psychologist
Associate Investigator(s):	Dr Paul Morris, Lecturer, the University of Edinburgh (Academic Supervisor) Prof Kevin Power, Head of NHS Tayside Psychological Therapies Service (Clinical Supervisor) Dr Devesh Dhasmana, Respiratory Consultant, NHS Fife (Principal Investigator) Dr Rekha Chaudhuri, Associate Specialist and Hon Clinical Associate Professor, NHS Greater Glasgow and Clyde (Principal Investigator) Dr Freda Yang, Research Fellow, NHS Greater Glasgow and Clyde (Associate Investigator)
Location:	NHS Fife, NHS Greater Glasgow and Clyde

Declaration by Participant

- I confirm that I have read and understood the information sheet dated 4 November 2019 (Version 6) for the above study. I have had opportunity to consider the information, ask questions and I am satisfied with any answers I have received.

- I understand that my participation is voluntary and that a decision not to take part will not affect the standard of my medical care or legal rights.

- I agree that unidentifiable data gained from the study can be reused to assist other reviews or research conducted in the public interest.

Please continue to the questionnaire part of the study pack only if you have read and understood the above statements and agree to take part in the study.

If you decide to go ahead, complete and return the questionnaires, it will be assumed that you are giving your consent to take part.

This consent form is yours to keep.

Study Title: What psychological factors influence asthma outcomes?

Demographic Information Sheet

Please answer the questions below:

Age: _____

Gender: Male/Female/Other

If Other, how do you describe your gender? _____

Your **Weight:** _____

Your **Height:** _____

Are you:
- ☐ Currently a smoker
- ☐ An ex-smoker
- ☐ Someone who has never smoked

If you currently smoke, how many cigarettes a day on average?: _____

How long have you lived with asthma?: _____ **years**

Have you had to go into hospital due to your asthma in the past year? YES/NO
(If yes), please tell us how often: _____

Have you had to go to A&E due to your asthma in the past year? YES/NO
(If yes), please tell us how often: _____

How many courses of steroid medication have you had in the past year?
- ☐ 0
- ☐ 1-3
- ☐ 4 or more

How many puffs of your short-acting reliever inhaler have you taken in the past week?
_____ **(please estimate if you can't remember exactly)**

(please turn to continue to questionnaires)

QUESTIONNAIRES **Date completed: _____**

Patient Health Questionnaire 9 (PHQ-9) Over the **last 2 weeks**, how often have you been bothered by any of the following problems? Please circle an option that applies to you.		Not at all	Several days	More than half the days	Nearly every day
1	Little interest or pleasure in doing things	0	1	2	3
2	Feeling down, depressed, or hopeless	0	1	2	3
3	Trouble falling or staying asleep or sleeping too much	0	1	2	3
4	Feeling tired or having little energy	0	1	2	3
5	Poor appetite or overeating	0	1	2	3
6	Feeling bad about yourself – or that you are a failure or have let yourself or your family down	0	1	2	3
7	Trouble concentrating on things, such as reading or watching television	0	1	2	3
8	Moving or speaking so slowly that other people could have noticed? Or the opposite – being so fidgety or restless that you have been moving around a lot more than usual	0	1	2	3
9	Thoughts that you would be better off dead or hurting yourself in some way	0	1	2	3
		PHQ-9 score			

Generalised Anxiety Disorder (GAD-7) Over the **last 2 weeks**, how often have you been bothered by any of the following problems? Please circle an option that applies to you.		Not at all	Several days	More than half the days	Nearly every day
1	Feeling nervous, anxious or on edge	0	1	2	3
2	Not being able to stop or control worrying	0	1	2	3
3	Worrying too much about different things	0	1	2	3
4	Trouble relaxing	0	1	2	3
5	Being so restless that it is hard to sit still	0	1	2	3
6	Becoming easily annoyed or irritable	0	1	2	3
7	Feeling afraid that something awful might happen	0	1	2	3
		GAD-7 score			

Date completed: _____

Brief Experiential Avoidance Questionnaire (BEAQ)

1----------2----------3----------4----------5----------6

Strongly Disagree | Moderately Disagree | Slightly Disagree | Slightly Agree | Moderately Agree | Strongly Agree

	Please circle how much you agree or disagree with each statement.	Strongly Dis	Mod Dis	Slightly Dis	Slightly Agree	Mod Agree	Strongly Agree
1	The key to a good life is never feeling any pain	1	2	3	4	5	6
2	I am quick to leave any situation that makes me feel uneasy	1	2	3	4	5	6
3	When unpleasant memories come to me, I try to put them out of my mind	1	2	3	4	5	6
4	I feel disconnected from my emotions	1	2	3	4	5	6
5	I won't do something until I absolutely have to	1	2	3	4	5	6
6	Fear of anxiety will not stop me from doing something important	1	2	3	4	5	6
7	I would give up a lot not to feel bad	1	2	3	4	5	6
8	I rarely do something if there is a chance that it will upset me	1	2	3	4	5	6
9	It's hard for me to know what I'm feeling	1	2	3	4	5	6
10	I try to put off unpleasant tasks for as long as possible	1	2	3	4	5	6
11	I go out of my way to avoid uncomfortable situations	1	2	3	4	5	6
12	One of my big goals is to be free from painful emotions	1	2	3	4	5	6
13	I work hard to keep out upsetting emotions	1	2	3	4	5	6
14	If I have any doubts about doing something, I just won't do it.	1	2	3	4	5	6
15	Pain always leads to suffering	1	2	3	4	5	6
		BEAQ score					

Date completed: _____

Perceived Control of Asthma Questionnaire (PCAQ)

1----------2----------3----------4----------5
Strongly Agree Agree Neutral Disagree Strongly Disagree

	Please circle how much you agree or disagree with each statement.	Strongly Agree	Agree	Neutral	Disagree	Strongly Disagree
1	I can reduce my asthma by staying calm and relaxed.	1	2	3	4	5
2	Too often, my asthma just seems to hit me out of the blue.	1	2	3	4	5
3	If I do all the right things, I can successfully manage my asthma.	1	2	3	4	5
4	I can do a lot of things myself to cope with my asthma.	1	2	3	4	5
5	When I manage my personal life well, my asthma does not affect me as much.	1	2	3	4	5
6	I have considerable ability to control my asthma.	1	2	3	4	5
7	I would feel helpless if I could not rely on other people for help when I am not feeling well from asthma.	1	2	3	4	5
8	No matter what I do, or how hard I try, I just cannot seem to get relief from my asthma.	1	2	3	4	5
9	I am coping effectively with my asthma.	1	2	3	4	5
10	It seems as though fate and other factors beyond my control affect my asthma.	1	2	3	4	5
11	Asthma is controlling my life.	1	2	3	4	5
		PCAQ score				

Date completed: _____

Asthma Control Test (ACT)

For each question, please circle the number which best applies to you.

1	During the past 4 weeks, how often did your asthma prevent you from getting as much done at work, school/college or home?	1 – All time 2 – Most of the time 3 – Some of the time 4 – A little of the time 5 – None of the time
2	During the past 4 weeks, how often have you had shortness of breath?	1 – More than once a day 2 – Once a day 3 – 3-6 times a day 4 – 1-2 times a week 5 – Not at all
3	During the past 4 weeks, how often did your asthma symptoms (wheezing, coughing, chest tightness, shortness of breath) make you wake up at night or earlier than usual in the morning?	1 – 4 or more times a week 2 – 2-3 nights a week 3 – Once a week 4 – Once or twice 5 – Not at all
4	During the past 4 weeks, how often have you used your reliever inhaler (usually blue)?	1 – 3 or more times a day 2 – 1-2 times daily 3 – 2-3 times a week 4 – Once a week or less 5 – Not at all
5	How would you rate your asthma control during the past 4 weeks?	1 – Not controlled 2 – Poorly controlled 3 – Somewhat controlled 4 – Well controlled 5 – Completely controlled
		ACT score:

MINI ASTHMA QUALITY OF LIFE QUESTIONNAIRE

Please complete **all** questions by circling the number that best describes how you have been during the **last 2 weeks as a result of your asthma.**

IN GENERAL, HOW MUCH OF THE TIME **DURING THE LAST 2 WEEKS** DID YOU:

		All of the Time	Most of the Time	A Good Bit of the Time	Some of the Time	A Little of the Time	Hardly Any of the Time	None of the Time
1.	Feel SHORT OF BREATH as a result of your asthma?	1	2	3	4	5	6	7
2.	Feel bothered by or have to avoid DUST in the environment?	1	2	3	4	5	6	7
3.	Feel FRUSTRATED as a result of your asthma?	1	2	3	4	5	6	7
4.	Feel bothered by COUGHING?	1	2	3	4	5	6	7
5.	Feel AFRAID OF NOT HAVING YOUR ASTHMA MEDICATION AVAILABLE?	1	2	3	4	5	6	7
6.	Experience a feeling of CHEST TIGHTNESS or CHEST HEAVINESS?	1	2	3	4	5	6	7
7.	Feel bothered by or have to avoid CIGARETTE SMOKE in the environment?	1	2	3	4	5	6	7
8.	Have DIFFICULTY GETTING A GOOD NIGHT'S SLEEP as a result of your asthma?	1	2	3	4	5	6	7
9.	Feel CONCERNED ABOUT HAVING ASTHMA?	1	2	3	4	5	6	7
10.	Experience a WHEEZE in your chest?	1	2	3	4	5	6	7
11.	Feel bothered by or have to avoid going outside because of WEATHER OR AIR POLLUTION?	1	2	3	4	5	6	7

HOW **LIMITED** HAVE YOU BEEN **DURING THE LAST 2 WEEKS** DOING THESE ACTIVITIES **AS A RESULT OF YOUR ASTHMA?**

		Totally Limited	Extremely Limited	Very Limited	Moderate Limitation	Some Limitation	A Little Limitation	Not at all Limited
12.	STRENUOUS ACTIVITIES (such as hurrying, exercising, running up stairs, sports)	1	2	3	4	5	6	7
13.	MODERATE ACTIVITIES (such as walking, housework, gardening, shopping, climbing stairs)	1	2	3	4	5	6	7
14.	SOCIAL ACTIVITIES (such as talking, playing with pets/children, visiting friends/relatives)	1	2	3	4	5	6	7
15.	WORK-RELATED ACTIVITIES* (tasks you have to do at work)	1	2	3	4	5	6	7

*If you are not employed or self-employed, these should be tasks you have to do most days.

PRIZE DRAW

Prize draw number_____

Please tick the following box if you would like to be included in a prize draw for a chance to win one of two £50 gift cards of your choice (Amazon/Tesco/Boots/Sainsburys/ASDA/John Lewis). ☐

(This page will be used for prize draw purposes only and will be detached from questionnaires on receipt)

DEBRIEF SHEET

Study: What psychological factors influence asthma outcomes?

Thank you for participating in completing the questionnaires for the above study. We hope that you have found it interesting and have not been upset by any of the topics covered.

However, if you have found any part of this experience to be distressing or you are concerned about your asthma/or mental health and you wish to speak to someone, please contact your **GP or your clinical asthma team.** There are also several voluntary and NHS organisations listed below that you can contact for an expert and confidential support or advice:

Samaritans Confidential support for people experiencing feelings of distress or despair. Phone: 116 123 (free 24-hour helpline) Website: www.samaritans.org.uk	**Breathing Space** Free and confidential support and signposting service aimed at people who are feeling sad or depressed. Phone: 0800 83 85 87 (Mon-Thu, 6pm to 2am; Weekend: Fri 6pm – Mon 6am)
Anxiety UK Charity providing support for people experiencing anxiety. Phone: 03444 775 774 (Mon-Fri, 9.30am-5.30pm) Website: www.anxietyuk.org.uk	**Rethink Mental Illness** Support and advice for people living with mental illness. Phone: 0300 5000 927 (Mon-Fri, 9.30am-4pm) Website: www.rethink.org
SANE Emotional support, information and guidance for people affected by mental illness. SANEline: 0300 304 7000 (daily, 4.30-10.30pm) Website: www.sane.org.uk/support	**Asthma UK Helpline** Advice and information about asthma and asthma management. Phone: 0300 222 5800 (Mon-Fri, 9am -5pm) Website: asthma.org.uk

If you have any further questions about the study, please contact Lucie Michalova via Linda Scott on: 01382 346160 or email:

This debrief sheet is yours to keep.

THANK YOU FOR YOUR PARTICIPATION

PRIZE DRAW If you agreed to be included in the prize draw, **please retain this slip** or write down your Prize draw number and keep it somewhere safe. The draw will take place on **29th May 2020** and the winning numbers will be published on the project website on the same day with details of how to get in touch to claim the prize. Winners will have until 30th June 2020 to get in touch.

My Prize draw number _____ **Study website:** https://www.wiki.ed.ac.uk/x/W_xlFQ

APPENDIX M: Study Protocol

Generalised anxiety and asthma outcomes: the contributing role of self-efficacy and experiential avoidance

Protocol: V6 13 November 2019

Chief Investigator

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Introduction

Asthma is a long-term health condition which is caused by obstruction of the airways due to inflammation (Global Initiative for Asthma guidelines, 2009). Despite asthma being a condition that can be managed very successfully through self-management and medication, it is estimated that in the UK around 1200 people a year die because of asthma (Taylor et al., 2014) and more than 50% live with asthma which is poorly controlled (Braido et al., 2016). Poor asthma control was associated with worse outcomes with regards to mortality, asthma-related quality of life (QoL) and higher utilization of health services in UK sample of adult asthmatics (Braido et al., 2016). This highlights the need for a better understanding of factors that hinder effective asthma control and QoL to reduce unnecessary asthma-related personal/economic burden and mortality.

In recent years it has become apparent that psychological factors can explain an important proportion of variance in asthma outcomes (Di Marco et al., 2010; Deshmukh et al., 2007). Generalised anxiety (anxiety characterized by the presence of unspecified, frequent and uncontrollable worries) has shown to be particularly prevalent in this population compared to individuals without asthma diagnosis (Lavoie et al., 2011; Weiser, 2007). Higher levels of generalised anxiety have been linked to poorer asthma outcomes such as asthma control, diminished asthma-related QoL and higher use of health care utilization (Di Marco et al., 2010; Feldman et al., 2005; Lavoie et al., 2011). Despite these preliminary findings, limited number of studies have looked at the association between generalised anxiety and asthma outcomes and only a handful have investigated a range of asthma outcomes indicators within the same study (e.g. asthma control and asthma QoL) (e.g. Lavoie et al., 2011, Fernandes et al., 2010). This is crucial as an individual who reports stable and well-managed asthma might still experience poor asthma-related well-being (Deshmukh et al., 2007).

Also, most studies looking at generalised anxiety in asthma employed a diagnostic interview as a method of exploring co-morbid generalised anxiety disorder (GAD). Although a valid measure, it can be argued that it doesn't account for subthreshold levels of generalised anxiety, which are also likely to be clinically relevant with regards to asthma-related behaviours and outcomes. Using more general measure might be therefore useful to capture a variance in anxiety scores amongst individuals with asthma. Compared to diagnostic interview, a quick GAD screen measure is also more likely to be used in routine clinical practice, given current NHS economical and time pressures.

As mentioned above, previously published studies highlighted that paying attention to psychological factors such as anxiety in asthma population is crucial as it showed to be linked to poorer asthma outcomes (please see Di Marco et al., 2010 for a review). However, less is

known in the literature about the underlying mechanism which can explain this relationship. The association between anxiety and asthma outcomes is complex. As such, it is likely to be influenced by other factors which might co-occur with high anxiety and change or explain its association with asthma morbidity (a relationship known as mediation).

One important factor that may partially explain the link between anxiety and asthma-related outcomes is individual's perceived ability to manage their asthma, construct known as self-efficacy (Bandura, 1994). A previous study by Lavoie et al (2011) found that amongst individuals with asthma, higher levels of GAD were associated with lower self-reported self-efficacy to manage asthma. Many studies found that low levels of asthma-specific self-efficacy were in turn associated with worse overall asthma control, greater frequency of short-acting reliever medication use and poorer asthma-related quality of life (Lavoie, 2008; Manusco et al. 2010; Martin, 2009; Chen, 2010; Lavoie et al., 2010). However, to date, only one study has explored self-efficacy as a potential factor influencing the relationship between generalised anxiety and poor asthma morbidity.

Another potential factor which might offer an explanation about how generalised anxiety contributes to asthma outcomes is experiential avoidance (a tendency to cope with unpleasant internal experiences including emotions, thoughts and bodily sensations by trying to change or avoid them). Emotion-focused strategies such as avoidance have been shown to predict poorer health outcomes whilst acceptance and more active coping strategies have been shown to have a positive effect on illness-related outcomes (Lazarus & Folkman, 1984; Bombardier et al., 1990). It was previously indicated that individuals with generalised anxiety have a lower ability to regulate unpleasant internal experiences and are more likely to engage in experiential avoidance (Buhr and Dugas, 2012; Mennin et al., 2002).

Previous studies showed that individuals who scored higher on experiential avoidance were more likely to report poorer medication compliance and disease control in other chronic illnesses such as HIV and diabetes (Chartier et al., 2010; Weijman, Ros, & Rutten, 2005). Avoidance of internal experiences has also been repeatedly associated with worse well-being and health-related QoL (e.g. Hayes et al., 2004). Some preliminary research findings using an asthma population suggested that higher levels of experiential avoidance were shown to negatively affect self-reported asthma-related QoL (Stavrinaki et al., 2013; unpublished study). However, much of the research looking at experiential avoidance is limited using the Acceptance and Commitment Questionnaire (AAQ-I, Hayes et al., 2004; revised AAQ-II, Bond et al., 2011) widely criticised for its poor psychometric properties and discriminant validity (Chawla & Ostafin, 2007; Gámez et al., 2011; Wolgast, 2014).

Despite previous research suggesting that affective regulatory processes should be considered as an important factor influencing the relationship between distress and health outcomes, no published study to date has explored whether high levels of experiential avoidance influence the relationship between levels of generalised anxiety and indicators of asthma morbidity in adults with asthma.

In order to address some of the gaps in previous research and literature and to further develop an evidence base for the role of psychological factors on asthma-related outcomes, the current study aims to investigate the direct relationship between generalised anxiety and asthma morbidity indicators (asthma control, use of reliever asthma medication, asthma QoL) in adults with asthma and whether individuals' confidence in managing their asthma and their tendency to avoid unpleasant internal experiences mediate this relationship. The current study will also try to address previous methodological limitations by employing more recently developed Brief Experiential Avoidance Questionnaire (BEAQ) (Gámez et al., 2014) as a measure of experiential avoidance. This measure has shown good psychometrics and thus might represent a more suitable measure to address AAQ limitations. The current study will also employ a self-reported measure of GAD (7-item Generalised Anxiety Disorder Questionnaire) to investigate its predictive validity in the sample of adults with asthma.

We hypothesise that:

(1) In adults with asthma, higher levels of co-morbid generalised anxiety will be associated with poorer asthma morbidity indicators (poorer asthma control, higher use of reliever asthma medication and poorer asthma quality life), lower self-efficacy to manage asthma and greater experiential avoidance.

(2) In adults with asthma, Self-efficacy and Experiential avoidance will contribute to the explanation of the relationship between generalised anxiety and poorer asthma morbidity indicators (asthma control, use of reliever asthma medication and asthma quality life).

Methods

Recruitment

An opportunistic sample of 100 - 120 patients will be recruited from the outpatient asthma clinics in NHS Fife and NHS Greater Glasgow and Clyde.

Power Calculations

Using G*power 3.0.10 (Faul, Buchner, Erdfelder & Lang, 2008), a priori power calculation estimated that employing a hierarchical multiple regression analysis with 6 control and 1 test predictors (total of 7 predictors), a sample of 89 participants will be required to detect a medium effect size (.15) with a power of .95 (alpha set at .05). The researcher will aim to recruit 100 - 120 participants to allow for a higher amount of attrition. This sample size was deemed enough for a subsequent mediation analyses using a bootstrapping approach. In accordance with recommendations by Fritz & MacKinnon (2007), it has been estimated that for this analysis a sample size of 71 will be required to achieve a power of 0.8 to detect a medium effect size of the indirect effect.

Eligibility criteria

Inclusion criteria:

Identified by clinician:

- Primary diagnosis of asthma
- Aged 16 - 75 years
- Receiving medical treatment for asthma for at least 6 months
- Good written and spoken understanding of English language

Exclusion criteria:

Identified by clinician:

- Diagnosis of a pulmonary disorder presenting higher morbidity than asthma (e.g., chronic cystic fibrosis, chronic obstructive pulmonary disease, HIV-related lymphocytic airway inflammation)
- Apparent cognitive or language deficit

Self-reported by participants:

- Currently experiencing an episode of a serious mental illness, e.g. psychosis
- Self-reported current misuse of alcohol or drugs
- diagnosis of Fibromyalgia

Identification of participants

Eligible participants will be identified by their current respiratory clinicians (either respiratory consultants or respiratory nurses) working in the outpatient respiratory departments in NHS Fife and NHS Greater Glasgow and Clyde. Clinicians will be provided with the inclusion and exclusion criteria as well as information about the study and they will screen all potential participants to ensure that patients not meeting the study criteria are excluded. This will involve speaking to participants and checking their medical file. At the end of their routine consultation

session, clinicians will be asked to briefly discuss the current study with eligible participants and check their willingness to participate. If participants show a preliminary interest, the clinician will provide them with a study pack.

A first section of the study pack will include an information sheet about the study. This section will clearly state the rationale of the study, what it will entail and confidentiality guidelines. It will also screen participants for additional exclusion criteria: current alcohol and drug abuse, current episode of serious mental health difficulties e.g. psychosis and diagnosis of Fibromyalgia. These exclusion criteria will be self-reported as patient's might not feel comfortable to disclose these to clinicians due to stigma and might not be included in their patient file. If participants are excluded at this point and they wish to discuss this further the information sheet will advise them to contact the Chief Investigator on the contact details included. The information sheet will also make participants aware that participation is voluntary, their participation/non-participation will not affect the care they receive and that they can withdraw from the study at any point until the end of the data collection period. It will clearly state Chief Investigator's contact details if participants wish to discuss the study in more details prior to participation. To fully consider their participation, participants can decide to complete the pack at any time from receiving the pack until the end of the study.

Questionnaires and consenting procedure

In the research pack, potential participants will be told that they are being invited to take part in a research project about the impact of psychological factors on asthma outcomes. They will be informed that, should they wish to participate, they will be asked to provide some basic information about themselves such as age, gender and their asthma. After this, they will be asked to complete 6 short questionnaires about their anxiety, mood, asthma related QoL, the way they manage emotions, their perceived confidence in managing asthma and questions about their current asthma management. The completion of the questionnaires should take on average about 20 minutes. Potential participants will be advised that they will be asked to fill these questionnaires only once and they can choose to either fill them once in the hospital and return them to the reception or take them home and when completed post them pack in a prepaid envelope. They will be advised that they can take part at any point until the end of the study collection period. The last study packs will be distributed no less than one week before the end of the study collection period to give all participants at least one week to consider participation and to take part.

Before taking part, participants will be asked to carefully read the provided information sheet and decide whether they would like to participate. In the consent form, participants will

be asked to read statements that ensure that they read the information sheet, understand what the study involves and agree to take part. Only then, the participants will be asked to continue with the questionnaire part of the study pack. Participants will be made aware that if they decide to go ahead and complete and return the questionnaires, it will be assumed that they are giving their consent to take part. It is estimated that reading the information sheet and providing a consent should not take longer than 10 minutes.

Procedure

A total of 100-120 patients who currently receive treatment for asthma will be recruited from the outpatient respiratory departments in NHS Fife and NHS Greater Glasgow and Clyde. Clinicians will identify participants from their current caseloads using provided inclusion and exclusion criteria. This will involve speaking to participants and checking their medical file, where this is necessary to confirm inclusion/exclusion criteria. Eligible participants who are willing to participate will be provided with a study pack. They will be asked to complete the study pack in their own time. Participants who read and understood the study information and associated consent form and decided to take part will be asked to provide basic demographic and asthma related information and 6 questionnaires. Selected measures were chosen with an intention of reducing unnecessary participation burden. Brief versions of measures were chosen were available. The completion of the following procedure is estimated to take around 20 minutes in total. Participants will be asked to complete the questionnaires once only.

The procedure will include the following:

- **The Demographic form** which was developed by the researcher. The form collects basic demographic information, including participant's age, sex, height and weight (to calculate BMI), smoking status, number of cigarettes smoked/day and number of years living with asthma, short-acting reliever inhaler usage in the last week (defined as a number of inhalations in the last week), number of courses of steroid medication in the past year and number of A&E visits and hospitalizations in the past year. *Average completion time: 3 minutes*
- **The Generalised Anxiety Disorder 7 (GAD – 7) questionnaire** (Spitzer, Kroenke, Williams & Löwe, 2006) which is a self-report questionnaire designed to assess the occurrence of anxiety symptoms in the last two weeks. GAD-7 showed to be internally consist ($\alpha = .92$) and reliable (test-retest) (ICC = .83) (Spitzer et al., 2006). Participants are asked to rate their experience of anxiety symptoms on a 4-point Likert scale ranging from 0 = not at all to 3 = nearly every day). The total score is derived as the sum of scores (range 0 to 21). Scores can be divided into the following anxiety severity levels: mild = ≥ 5, moderate = ≥ 10 and severe = ≥ 15. A score above

10 has been used as a cut-off indicating the presence of anxiety disorder (Williams, 2014). Given the frequent overlap between anxiety and depression, a factorial analysis was conducted to assess GAD-7 alongside a measure of depression: Patient Health Questionnaire (PHQ-9) (Spitzer et al., 2006). All GAD-7 items showed highest factor loading on factor one compared to all depression items that showed the highest loading on factor two, demonstrating that GAD-7 measures distinct construct from depression. *Average completion time: 2 minutes*

- **Patient Health Questionnaire (PHQ-9)** (Spitzer et al., 1999). As depression is a common co-morbidity in individuals with generalised anxiety and was previously shown to be related to asthma morbidity, the current study will examine levels of depression in the current sample. The PHQ-9 (Spitzer et al., 1999) is a 9-item self-report questionnaire and will be used to assess depressive symptoms. Sum of scores is used to obtain a total score (range 0 to 27). A higher score indicates a greater occurrence of depressive symptoms. PHQ-9 demonstrated good internal consistency ($\alpha = 0.90$) (Spitzer et al., 1999). *Average completion time: 2 minutes*
- **The Perceived Control of Asthma Questionnaire (PCAQ)** (Katz, Yelin, Eisner and Blanc, 2002) will be used to measure individuals' perceived ability to manage their asthma. The PCAS is an 11-item self-report measure. Responses are scored on a 5-point Likert scale ranging from 1 - strongly agree to 5 - strongly disagree. In previous research using a sample of adult asthmatics, the PCAQ showed good internal consistency (.79) and construct validity (Katz, Yelin, Eisner and Blanc, 2002). Previous studies have found an association between PCAQ and asthma-specific QoL (using mini Asthma-Specific Quality of Life Questionnaire) and asthma control (using Asthma Control Questionnaire) (Katz, Yelin, Eisner and Blanc, 2002; Olajos-Clow, Costello and Lougheed, 2005). *Average completion time: 3 minutes*
- **Brief Experiential Avoidance Questionnaire (BEAQ)** (Gámez et al., 2014) is a briefer version of the original well validated Multidimensional Experiential Avoidance Questionnaire (MEAQ) (Gámez et al., 2011). BEAQ consists of 15 items assessing experiential avoidance – defined as a coping style used to regulate unpleasant internal experiences (including feelings, thoughts and physical sensations) which ranges from acceptance to avoidance (Machell, Goodman & Kashdan, 2014). In the original evaluation study, BEAQ exhibited good internal consistency with Cronbach alphas ranging from .80 -.86 across clinical, community and student samples. What more, in a recent study using a sample of chronic illness population (patients with cancer) BEAQ showed good test-retest reliability ($r = .85$) (Carr, 2014). *Average completion time: 4 minutes*
- **Mini Asthma Quality of Life Questionnaire (MiniAQLQ)** (Juniper et al., 1999) is a shorter 15-item version of the well-established and validated AQLQ (Juniper et al. 1992). It is designed to assess the impact of asthma on QoL across four domains in the past two weeks: asthma

symptomatology, limitation of activities, emotions and environment. Individuals are asked to rate their responses on a 7-point Likert scale (ranging from 1 = severe impairment to 7 = no impairment). In the development and validation study by Juniper et al. (1999) MiniAQLQ showed good internal consistency for the total and individual domain scores (.80 - .89) and a good ability to detect change over time. In a study using a sample of adults with physician-diagnosed asthma, the MiniAQLQ showed Cronbach alpha of .90, .67, .84 and .94 for the symptoms, environment, emotions and limitation of activities subscales respectively (Avallone et al., 2011). *Average completion time: 3 minutes*

- **Asthma Control Test (ACT)** (Schatz, 2006) is a 5-item self-administered and validated questionnaire looking at individuals' level of asthma control over the past 4 weeks. Self-reported items are rated on 5-point Likert scale ranging from 1=poor control to 5=good control. Total ACT score is obtained by summing up scores on all 5 items and ranges from 5-25. In the analysis, Asthma Control Test score will be expressed as a continuous variable where higher scores indicate better control. The 3 levels of ACT scores where ACT score ≥20 identifies well-controlled asthma, score 16-19 not well controlled and < 16 indicating very poorly controlled asthma, will be calculated to gain a better understanding about the sample. The ACT showed high internal reliability consistency (0.85) in a sample of adult asthmatics attending asthma specialist clinic (Schatz et al, 2006). Similarly, Nathan et al. (2004) reported high internal consistency of the ACT score with specialists' ratings among subjects with controlled asthma as well as subjects with uncontrolled asthma (0.79 and 0.83, respectively). ACT was also found to have a good test-retest reliability (0.77) (Alvarez-Gutie´rrez et al., 2010). ACT showed high correlation with other validated asthma control measure – Asthma Control Questionnaire (r = .89) (Schatz et al., 2006). *Average completion time: 3 minutes*

The final section of the study pack will contain information about the aims of the study to ensure participants fully understood the purpose of their involvement. It will also contain Chief Investigator's contact details if participants wish to ask any questions regarding the study. It will outline that participants should contact their GP, current asthma team or 3rd sector voluntary organisations (list provided) if they become concerned about their mental health or asthma. The final page will thank participants for taking part in the study and provide a web link to a project wiki page (https://www.wiki.ed.ac.uk/x/W_xlFQ) which will have details of study results with an approximate timescale when these results will be available for viewing. Study results will be available in an easy to read standardised abstract format together with downloads for any suitable reports or other outputs such as publications.

It will also include information about a prize draw and ask participants to retain a slip including their allocated prize draw number or to write it down somewhere safe. Individuals

who participated before 20th December, the original end of the recruitment period, will be made aware that the prize draw will take place on 20th January 2020. The winning numbers will be published on the project wiki page (https://www.wiki.ed.ac.uk/x/W_xlFQ) on the same day with details of how to get in touch to claim the prize. Winners will be made aware that they have until 20th February 2020 to get in touch. Participants will be advised that if they lost the details of the project website or do not have access to the internet, they can get in touch with the Chief Investigator using included contact details.

To reflect the extension of recruitment period from 21st December 2019 until the end of April 2020, participants who are recruited within this period, will receive updated study documentation and will be included in an additional prize draw which will include additional vouchers. The updated documentation will include details of the additional prize draw date (29th May 2020) and the deadline to claim the prize (30th June 2020). The additional prize draw will follow the same procedure as the previous one with regards to the type of prizes, publishing of winning numbers and claiming of prizes.

Analysis

Group characteristics

The group characteristics will firstly be reported. The proportion of male and female participants and participants who smoke will be calculated together with means and standard deviations for age, years of living with asthma, cigarettes smoked a day, BMI, frequency of A&E visits and hospitalizations in the past year, number of inhalations in the last week (short-acting reliever inhalator usage). Additional descriptive statistics will be calculated in percentages for discrete demographic variables, including courses of steroid medication in the last year ('0', '1-3', '4 or more') and smoking status ('current smoker', 'ex-smoker', 'never smoked'). Means and standard deviations will be calculated for quantitative variables, including level of GA (GAD-7 score), depression (PHQ-9 score), experiential avoidance (BEAQ score), perceived control of asthma (PCAQ score), QoL (MiniAQLQ score), asthma control (ACT score).

Exploratory analyses: the relationship between predictor and outcome variables

Correlations will be calculated to explore relationships between predictor and outcome variables. The Pearson product correlation coefficient for parametric data or the Spearman's rank correlation coefficient for non-parametric data will be used to explore the strength of the relationship between the predictor and outcome variables. The absolute value of the correlation

coefficient will be taken to represent the following effect sizes: small for values >0.3, medium for values between 0.3-0.5 and large for values <0.5 (Cohen, 1988). Only variables that significantly correlate with the outcome variables will be included in subsequent regression analyses.

The relationship between generalised anxiety and asthma outcomes

To test the relative strength of generalised anxiety in predicting indicators of asthma morbidity at time 1 (asthma control, asthma-specific QoL and frequency of use of short-acting asthma reliever medication), a simultaneous forced entry linear regression model will be calculated for each outcome variable, yielding three models in total. The forced entry method allows to test the exploratory power for the hypothesised variable whilst controlling for other variables in the equation. This is a preferred method for making predictions for new models since it allows to weigh the relative contribution of each variable without making prior assumptions regarding their importance (Field, 2003). In each of these analyses, independent variables will be entered in the following order (steps): (Step 1) control variables (age, sex, BMI, number of cigarettes smoked/day, number of years living with asthma and PHQ-9 total score) will be entered first to control for their potential confounding effect, followed by a test predictor (generalised anxiety) (Step 2). Indicators of asthma morbidity (asthma control, frequency of short-acting acting asthma reliever medication and asthma-specific QoL) will be entered as dependent variables. Analyses will be conducted using SPSS version 21 (IBM, Released 2012) or equivalent.

The influence of self-efficacy and experiential avoidance on the relationship between generalised anxiety and asthma outcomes

A series of mediation analyses (Preacher & Hayes, 2004) will be conducted using PROCESS macro MODEL 4 in SPSS (Hayes, 2013) or equivalent to investigate factors that were hypothesized to influence difference in asthma morbidity. Each of the mediation models will independently evaluate whether the relationship between generalised anxiety and indicators of asthma morbidity (asthma control, asthma-specific QoL, short-acting asthma reliever medication use) are influenced by individuals' perceived ability to manage their asthma and their levels of experiential avoidance.

Direct and indirect effects will be reported with 95% confidence intervals (CI) and p-values and will be considered statistically significant at p-value <.05. Following recommendations by Preacher and Kelley (2011) mediation effect sizes will be reported as magnitudes of the indirect effects compared to the maximum possible indirect effects (k^2) to better capture the full

meaning of indirect effects. According to Preacher and Kelley (2011) k^2 values of .1, .9 and .25 will indicate small, medium and large effect respectively. The current study will also report standardised regression coefficients (B) (measure for "a" coefficient) and partial correlations (r) (measure for "b" coefficient) to provide an indicator of effect sizes which can be compared with results from previous studies (MacKinnon, Fairchild & Fritz, 2007). Following Cohen (1988), B values of .14, .36 and .54 and r values of .1, .3 and .5 indicate small, medium and large effect respectively for each value. Preacher and Kelly (2011) noted that it is deemed appropriate to report multiple formats of effect sizes within the same study.

Application

Given the serious and adverse consequences of poorly controlled asthma, it is of great importance to improve our understanding of different factors influencing asthma outcomes. Accumulating evidence suggests that psychological factors can explain an important proportion of variance in asthma outcomes in adults with asthma. Previous studies have shown that generalised anxiety is particularly frequent in adults with asthma and can influence differences in asthma outcomes. However, the link between these is poorly understood. Although some preliminary evidence suggests that self-efficacy and differences in the way people perceive and manage emotions can provide some explanation regarding this link, it is yet to be investigated. The present study aims to fill this gap in the current research to expand our understanding of the impact of different psychological factors on asthma outcomes.

Findings from this study might encourage qualified professionals in asthma services to place more importance on taking psychological measures as part of the assessment process and on recognising how psychological factors might influence asthma-related outcomes. Psychological factors such as anxiety, self-efficacy and experiential avoidance are all modifiable factors which can be directly addressed through simple interventions. A better understanding of how these factors influence asthma morbidity can introduce an additional platform for asthma treatment, making it more effective. This could benefit asthma patient population as a whole by reducing the personal and physical burden of asthma and NHS services by reducing costs associated with poorly controlled asthma (e.g. increased medication use and greater health care utilization).

Lastly, as psychological research in this population is scarce, it is hoped that the current study will inspire future projects which will continue to add to the current evidence base and to the efforts of raising awareness of the impact of psychological factors on outcomes in this population.

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